Aspects socio-économiques et éco-épidémiologiques de l'échinococcose alvéolaire dans les communautés pastorales tibétaines en république populaire de Chine

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Aspects socio-économiques et éco-épidémiologiques de l'échinococcose alvéolaire dans les communautés pastorales tibétaines en république populaire de Chine.

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Personal Publications on this subject

1. *Qian Wang, Dominique A. Vuitton, Jiamin Qiu, Patrick Giraudoux, Yongfu Xiao, Peter M. Schantz, Francis Raoul, Tiaoying Li, Wen Yang, Philip S. Craig. 2004. Fenced pasture: a possible risk factor for human alveolar echinococcosis in Tibetan pastoralist communities of Sichuan, China. Acta Tropica 90: 285–293;*
2. *Qian Wang, Dominique A. Vuitton, Yongfu Xiao, Francis Raoul, Peter M. Schantz, Christine Budke, Wen Yang, Philip S. Craig, Patrick Giraudoux. Socio-economic and ecological correlates of alveolar echinococcosis emergence in Tibetan pastoralist communities. Emerging Infectious Diseases. Submitted.*
3. *Qian Wang, Dominique A. Vuitton, Qiu Jiamin, Wen Yang, Peter M. Schantz, Francis Raoul, Philip S. Craig, Patrick Giraudoux. Socio-economical and Behavioral Risk factors of Alveolar Echinococcocosis in Tibetan Communities, Sichuan Province, China. American Journal of Tropical Medicine and Hygiene. Submitted.*
4. *Wang Q, Qiu J.M, Schantz P, He J.G, Ito A, Liu F.J., 2001. Risk factors for development of human hydatidosis among people whose family is raising livestock in western Sichuan Province, China. Chin J Parasitic Dis Parasitol. 19:289-293.*
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6. *Vuitton D. A., Zhou S. Bresson-Hadni, Wang Q., Piarroux M., Raoul F. and Giraudoux P. 2003. Epidemiology of alveolar echinococcosis with particular reference to China and Europe. Parasitology. 127: S87–S107.*
7. *Christine M. Budke, Qiu Jiamin, Jakob Zinsstag, Wang Qian, and Paul R. Torgerson. 2004. Use of DISABILITY ADJUSTED LIFE YEARS in the estimation of the disease burden of Echinoccosis for a high endemic region of the Tibetan Plateau. Am. J. Trop. Med. Hyg., 71(1): 56–64.*

Résumé

Aspects socio-économiques et éco-épidémiologiques de l'échinococcose alvéolaire dans les communautés pastorales tibétaines en république populaire de Chine.

L'échinococcose alvéolaire (EA) est une zoonose importante, endémique dans l'hémisphère nord, en particulier dans plusieurs régions de l'ouest et du centre de l'Europe, la plupart des pays d'Asie centrale et orientale et quelques zones d'Amérique du Nord. Le métacestode d'*Echinococcus multilocularis* est l'agent pathogène de l'EA. Plusieurs espèces de petits mammifères sont les hôtes intermédiaires, hébergeant le métacestode (larve parasitaire), alors que des carnivores, tout particulièrement le renard, mais aussi le chien, servent d'hôte définitif au parasite et contaminent l'environnement par les œufs (oncosphères) infectants présents dans leurs fèces. Le foie est l'organe primitivement et majoritairement envahi par la larve parasitaire; des métastases sont également observées, en général à un stade évolué de la maladie, et peuvent être localisées dans n'importe quel organe ou tissu de l'hôte.

En RP de Chine, l'EA est un problème majeur de santé publique. Des patients atteints d'EA ont été recensés dans 8 Provinces et Régions Autonomes chinoises, la plupart étant dans les zones les moins développées des provinces du Heilongjiang, Gansu, Qinghai, et Sichuan, et des régions autonomes de Mongolie Intérieure et du Tibet, Hui du Ningxia et Ouigoure du Xinjiang. Dans la Province du Sichuan, l'EA est endémique dans les populations Tibétaines qui résident principalement à l'ouest de la

Province, sur les contreforts des hauts-plateaux tibétains. Environ 2 millions de Tibétains vivent dans la préfecture autonome tibétaine du Ganzi et la préfecture autonome tibétaine et Qiang d'Aba. Ces régions sont à une altitude d'environ 3500 mètres en moyenne, composées de hauts plateaux, de pâturages alpins et de vallées. Le climat, continental, est dominé par l'influence de la mousson. Les principales sources de revenu dans ces régions sont représentées par l'élevage, dans les communautés pastorales transhumantes, et l'agriculture, en particulier la culture de l'orge, dans les communautés agricoles rurales.

Dans la Province du Sichuan, les dépistages de masse dans les communautés en majorité tibétaines ont montré des prévalences pouvant atteindre 15 % (15/80) dans un village d'éleveurs, la prévalence moyenne étant de 1.9% (77/3998). Dans les communautés pastorales, la prévalence de la maladie évaluée par deux campagnes de dépistage de masse étaient respectivement de 5, 45% (44/809) et de 8,5% (60/705).

Des prévalences d'infection de 18% (prévalence estimée à partir d'une étude par purge à l'arécoline chez 371 chiens), 9.1% (4/44), et 44.4% (76/171) respectivement ont été trouvées chez les chiens appartenant aux familles, les chiens errants, et les renards tibétains. Des taux d'infection de 5.6% (13/233), 7.1% (1/14) et 25% (3/12) respectivement ont également été trouvés chez de petits lagomorphes de l'espèce *Ochotona curzoniae*, chez des lièvres de l'espèce *Lepus oiostolus*, et chez des rongeurs de l'espèce *Pitymis irene*. De nombreuses études ont été consacrées aux facteurs environnementaux, socio-économiques et comportementaux mettant les populations à risque d'être infecté par ce parasite. Cependant, peu de recherches ont abordé les facteurs socio-économiques et comportementaux contribuant à la transmission de l'EA dans les communautés Tibétaines.

Par comparaison avec les pays européens, où les renards sont considérés comme les sources majeures d'infection pour la transmission de l'EA à l'homme, les chiens semblent en Chine être les acteurs principaux de la contamination. Dans les communautés tibétaines, de nombreux facteurs socioéconomiques et comportementaux peuvent contribuer à favoriser l'interaction entre le chien et l'homme. Ces facteurs incluent l'élevage des bovins (yaks), des moutons et des chèvres, la religion bouddhique tibétaine, le nomadisme (ou la transhumance), le niveau général d'hygiène dans les communautés, vivant sous tente et itinérantes, et l'hygiène personnelle. Par ailleurs, il a été montré en Europe, et en particulier en France, et dans la province du Gansu et la région autonome Hui du Ningxia, en Chine, que des modifications paysagères pouvaient représenter un risque majeur d'intensification du fonctionnement du cycle parasitaire, et donc de la contamination potentielle humaine. Un certain type de paysage, par exemple les surfaces toujours en herbe (pâtures permanentes) ou les friches, est susceptible de promouvoir des cycles de pullulation de petits mammifères et donc d'augmenter le réservoir de parasites par augmentation du nombre des hôtes intermédiaires. Des études ont suggéré que le surpâturage pouvait être à l'origine de pullulations de petits mammifères dans les régions d'élevage du plateau tibétain, au Sichuan et au Qinghai. A l'occasion du travail de terrain réalisé dans les communautés pastorales tibétaines endémiques pour l'EA, nous avons fait l'hypothèse que le surpâturage, très dépendant du contexte socio-économique, pouvait être un des facteurs de modifications paysagères susceptibles de favoriser la transmission d'*E. multilocularis*, et que des changements récents dans la propriété du sol, amenant en particulier à enclore une partie des pâtures dans les zones habitées en hiver par ces communautés, pouvaient avoir aggravé la situation. Le but de notre recherche était donc d'explorer les facteurs socio-économiques et comportementaux intervenant dans la survenue de l'EA sur le plateau tibétain, et en particulier ceux qui, au plan communautaire, étaient susceptibles d'influencer, comme le surpâturage, les conditions environnementales et/ou écologiques de survenue de sa transmission à l'homme.

Pour répondre aux questions posées, nous avons utilisé des données provenant de deux types de sources:

1) des données épidémiologiques transversales, issues de 2 dépistages de masse réalisés pour l'un en 1997 et pour l'autre dans la période 2001-2003, coordonnés par l'Institut de Parasitologie du CDC du Sichuan, en collaboration avec des équipes de recherche internationales. Ces opérations de dépistages qui ont concerné 7138 personnes dans les Comtés, sites d'étude, comprenaient l'identification des cas d'EA par échographie du foie et par la sérologie utilisant le western-blot spécifique Em18, ainsi que le recueil des réponses à un questionnaire sur les facteurs de risques potentiels, et en particulier l'âge, le genre, le comté de résidence, le groupe ethnique, le niveau d'éducation, le nombre de chiens élevés par la famille, celui des chiens gardés par les voisins, le contact avec des peaux de renards, l'origine de l'eau de boisson, le nomadisme, le revenu global de la famille, la pratique de l'élevage, les

habitudes de lavage des mains avant de manger, de bouillir l'eau de boisson, de prévention des contacts entre les mouches et les aliments, et de jeu avec les chiens. La prévalence de la maladie a été mise en relation avec la surface de pâtures encloses à partir des données administratives fournies par les responsables de communes (piquets distribués par les autorités communales et vendus aux éleveurs).

2) des données de terrain obtenues en 2003, selon une méthodologie stricte d'échantillonnage, comprenant la densité en orifices de galeries des petits mammifères, utilisés comme indices indirect de présence, évaluée par transects, la mesure des zones effectivement encloses autour des résidences d'hiver (maisons ou tentes) des familles dans les communautés d'éleveurs transhumants, les réponses à un questionnaire sur les pratiques d'élevage, l'utilisation des pâtures encloses et des communaux, et le degré d'infection des chiens par *E. multilocularis*, mesuré par PCR sur le liquide fécal recueilli par purge à l'arécoline ou sur les fèces.

Notre étude a montré que la prévalence totale de l'EA était 3,1% (223/7138), que les femmes avaient une prévalence plus élevée (3,6%, 132/3713) que les hommes [2,7%, 91/3425; p=0,011; Odds Ratio (OR)= 1,44]. Les communautés pastorales (5,2%, 154/2955) avaient une prévalence plus élevée que les communautés agricoles (1,8%, 12/661) et que les communautés urbaines (2,1%, 49/2360). La prévalence était plus élevée dans le Comté de Shiqu.

Une analyse multivariée des facteurs de risque potentiels recueillis par questionnaire, chez les 7138 sujets examinés par ultrasonographie pour la présence de lésions d'EA, a montré que la prévalence augmentait significativement avec l'âge, dans toutes les communautés. Chez les éleveurs transhumants, la communauté avec la prévalence la plus haute de la maladie, seul le fait de ne pas éviter le contact des mouches avec les aliments, qui peut être interprété comme un indice de bas niveau d'hygiène de la famille, était un facteur de risque très significatif ($p < 0{,}001$; OR = 8,598). Dans les communautés agricoles, le nombre de chiens par famille ($p=0{,}0022$; OR=1,722) et la possession de peaux de renards ($p=0{,}017$; OR=6,583) étaient associés significativement à la prévalence de l'EA. Cependant ces deux facteurs étaient plus représentés dans le Comté de Shiqu, et ce fait pouvait rendre compte, au moins partiellement, de la différence de prévalence observée entre les Comtés. Dans les populations urbaines le sexe féminin, l'habitude de jouer avec les chiens ($p<0{,}004$; OR=4,550) et de boire de l'eau des ruisseaux (eau du robinet *versus* eau des ruisseaux: $p<0{,}001$; OR=0,276), étaient des facteurs de risque significatifs. Le rôle des chiens dans la transmission de l'EA en Chine a donc été confirmé, mais également, pour la première fois dans ce pays, un rôle direct du contact avec les renards a pu être montré. Une exposition au contact des chiens, appréciée par le nombre de chiens dans la famille et dans le voisinage, globalement égale pour toutes les familles et extrêmement élevée, peut être à l'origine de l'absence de corrélation trouvée entre cette exposition et la prévalence de la maladie, seuls des comportements différents vis-à-vis de l'hygiène étant susceptible de faire la différence entre les familles (et entre les malades et les sujets non contaminés).

Notre principale hypothèse de travail était le rôle potentiel du surpâturage comme facteur de risque de l'EA, car favorisant la pullulation de petits mammifères, hôtes intermédiaires, et donc augmentant l'infection des carnivores, hôtes définitifs. L'enquête par questionnaire, et les observations de terrain ont pu montrer qu'un pâturage illimité des troupeaux était permis sur les pâtures communales, alors que les pâtures encloses étaient protégées par la limitation de la durée de pâturage et du nombre de bêtes autorisées à y pâturer. Nos principaux résultats ont été les suivants: 1) le surpâturage existait dans les pâturages communaux sur le plateau Tibétain, comparés aux pâturages enclos; 2) si l'on comparait les pâturages enclos (non surpâturés) aux pâturages communaux, en dehors des clôtures (surpâturés), l'abondance des petits mammifères, estimée par méthode indiciaire (orifices des galeries) était significativement supérieure dans ces derniers, dans les fonds de vallées (p = 0,005), les entrées de vallées (p=0,005), et les plaines (p<0,001) (test non-paramétriques); 3) la clôture partielle des pâtures, en réduisant la surface utile de pâturages communaux, était associé à un surpâturage accru de ces communaux, responsable d'une augmentation de la densité de petits mammifères; par test de corrélation de Spearman, nous avons pu montrer que plus la surface enclose était importante, résultant en un surpâturage accru dans les communaux, plus la densité d'orifices de galerie des petits mammifères dans les communaux était élevée, quelque soit le paysage considéré: fonds de vallées (r_s = 0,382, p<0,001), plaines (r_s = 0,312, p<0,001), flanc de montagne (r_s = 0, 471, p<0,001), et entrée de vallée (r_s = 0, 296, p= 0,001); (4) le nombre médian d'indices de présence des petits mammifères était significativement associé, et de façon indépendante, à l'intensité de l'infection des chiens par *E. multilocularis* (p = 0,021; régression logistique pas à pas considérant l'âge et le sexe du chien et le type de collecte des échantillons (purge versus fèces).

Bien que le surpâturage soit un phénomène très étudié, en raison de son impact négatif important sur les conditions d'élevage et les revenus des éleveurs dans de nombreux pays du monde, autant que par ses effets néfastes sur l'environnement, une méthodologie satisfaisante pour sa mesure, en vue d'applications à des travaux de recherche scientifique, n'existe pas actuellement. Les relations entre surpâturage et densité des petits mammifères (rongeurs ou, comme sur le plateau tibétain, lagomorphes) sont très contradictoires dans la littérature, entre les régions étudiées, et même sur le même site d'étude…Ces contradictions peuvent en partie s'expliquer par l'absence de définition acceptée par tous de la notion de "surpâturage", et de la difficulté à le mesurer. Dans notre travail, il est apparu que le surpâturage existait à deux conditions, fondées sur un paradigme socio-économique: 1) les pâturages représentent une ressource limitée pour une communauté dont l'élevage est l'activité principale; 2) il existe des pâturages communaux dans cette communauté. Dans les communautés tibétaines, par ailleurs, il nous est apparu que la surface des pâtures encloses (devenues en quelque sorte "privées", même si ce terme ne recouvre pas la même réalité en Chine que dans les pays occidentaux), était corrélée au surpâturage dans les communaux, et aggravait donc la tendance naturelle au surpâturage des communaux dans ces régions.

Certaines imperfections dans notre méthodologie et dans la conduite de nos études, et qui devraient être corrigées par des travaux ultérieurs, peuvent être notées: 1) la réalisation des transects dans les sites d'habitation d'hiver des communautés tibétaines devrait tenir compte de l'ancienneté des clôtures, de la réelle propriété des zones encloses (une famille, partage par plusieurs familles…) et de plus de détails dans leur utilisation ; 2) notre hypothèse du rôle du surpâturage semble se confirmer pour les zones de résidence d'hiver; cependant, le rôle des pâturages d'été (qui sont entièrement des communaux) dans le maintien du cycle parasitaire et/ou la contamination humaine ne doit pas être négligé; 3) des études ultérieures devraient obligatoirement associer une identification précise des espèces de petits mammifères dans les différents habitats, ce qui exige un piégeage systématique dans les zones étudiées; 4) l'étude réalisée ne couvre qu'une surface très limitée du plateau tibétain, et des études analogues dans d'autres zones sont absolument indispensable pour tester la validité de l'hypothèse du surpâturage comme facteur de risque socio-économique et environnemental de l'EA dans cette partie du monde.

En conclusion, en raison vraisemblablement de comportements différents et d'une exposition environnementale différenciée, les facteurs de risques d'infection par *E. multilocularis* sur le plateau Tibétain varient selon les communautés et les stratégies de prévention et de contrôle devraient prendre en compte ces différences. Pour la première fois, le rôle direct d'un contact avec les renards a été mis en évidence dans les facteurs de risques de l'EA en Chine. En ce qui concerne les éleveurs, le surpâturage, aggravé par la clôture partielle des pâtures sur les territoires occupés en hiver par ces tibétains transhumants, est associé à une augmentation de la densité des petits mammifères, elle-même associée à une infection plus importante des chiens; cette série de conséquences en chaîne est vraisemblablement à l'origine de la corrélation entre la surface de pâtures enclose et la prévalence de l'EA dans les zones étudiées, au Sichuan. Pour la première fois, dans ces communautés pastorales du plateau tibétain, le surpâturage a été envisagé à partir d'un paradigme socio-économique. Les observations faites dans ce travail, sur les interactions entre facteurs de risque dans l'EA, sont un nouvel exemple de l'influence de facteurs socio-économiques et juridiques, en relation avec l'utilisation des sols par les communautés rurales, sur la prévalence d'une zoonose hautement dépendante de l'écologie des animaux, prédateurs et proies, qui jouent un rôle dans le fonctionnement d'un cycle parasitaire.

Summary

Socio-economical and eco-epidemiological aspects of alveolar echinococcosis in Tibetan pastoralist communities in P.R.China

Alveolar echinococcosis is a severe zoonosis that is widely endemic in north hemisphere, including regions in Western Europe, most of central Europe, central and eastern Asia and parts of North America. *Echinococcus multilocularis* (Em), the metacestode of the “fox tapeworm”, is the pathogenicity of Alveolar echinococcosis (AE). The intermediate hosts of the disease are small mammals and carnivores including foxes and dogs are the definitive hosts that discharge mature eggs with faeces. When human accidentally ingest the eggs, some may develop into disease, namely alveolar echinococcosis. The liver is the organ primarily affected; metastases are mainly observed in cases of advanced disease and may affect almost any organ.

In China, AE is major public health issue and patients were reported from 8 provinces and autonomous regions, namely Heilongjiang, Gansu, Qinghai, and Sichuan Provinces, Inner Mongolia, Ningxia Hui, Xinjiang Uygur and Tibetan Autonomous Regions. In Sichuan Province, AE is mostly endemic in Tibetan communities which are located in the west part of the Province. Tibetan communities in Sichuan Province are entirely located in the verge of east Qinghai-Tibet plateau. In the province, there are some 2 million Tibetan populations mostly inhabiting in Ganzi Tibetan Autonomous Prefecture and Aba Tibetan and Qiang Nationality Autonomous Prefecture. The landscape in the region features with high plateau mountain, alpine meadow, and valley. The weather in the 2 prefectures is characterized by a continent

monsoon plateau climate. The average altitude is around 3500 meter. Major industries in the region include livestock-raising in pastoralist communities and agriculture such as growing barley in agriculture communities.

In the Tibetan communities, AE is especially of concern. Past surveys showed that AE prevalence could be as high as 15% (12/80) in a herdsmen village, while the overall infection rate was 1.9% (77/3,998). The infection rate for herdsmen ranged from 5.45% (44/809) to 8.5% (60/705). In past surveys, owned dogs, stray dogs and Tibetan foxes were found to have high infection rates, 18% (an adjusted rate by a purgation study of 371 owned dogs), 9.1% (4/44), and 44.4% (76/171) respectively. *E. multilocularis* infection was also found among small mammals including *Ochotona curzoniae*, *Lepus oiostolus*, and *Pitymys irene*, with infection rates of 5.6% (13/233), 7.1% (1/14) and 25% (3/12) respectively. It thus appears that, in the Tibetan communities, the transmission cycle of *E.multilocularis* is functioning well. Past researches in other areas found various environmental, socio-economical and behavioral risk factors for AE prevalence. However, few researches tried to explore the socio-economical and behavior risk factors for AE/*E.multilocularis* transmission in the Tibetan region.

In comparison to European countries where foxes are viewed as major source of AE/*E.multilocularis* transmission, dogs are thought to be most significant source of the transmission in China. In the Tibetan communities, many socio-economical and behavior factors are assumed to strongly promote the interactions between humans and dogs. These factors include raising livestock, religion, nomadic, poor hygiene in communities as well as personal hygiene behaviors. Meanwhile, “landscape changes” were found to be a major AE/*E.multilocularis* transmission risk factor in Europe, particularly in France, and in Gansu Province and Ninxia Province, in China. Certain types of landscape, for example, bush or grassland, could promote high density of small mammals, which in turn may facilitate the AE/*E.multilocularis* transmission by increasing the intermediate host reservoir. There were previous studies suggesting that overgrazing could promote higher density of small mammals in Tibetan pastoralist regions in Sichuan and Qinghai provinces. Overgrazing, a concept deeply rooted in socio-economics, was assumed to be a factor for landscape change (grassland degradation) during field visit in Tibetan AE endemic pastoralist areas, which was further assumed to promote AE/*E.multilocularis* transmission. Therefore, our research also aimed at confirming the relationship between socio-economical and behavioral risk factors at the level of the community, and in particular overgrazing and its potential causes, and AE/*E.multilocularis* transmission.

For the purpose of the research, we used data from two sources:

1) *data from 2 cross-sectional epidemiological investigations*, one was done in 1997 and another was in the period from 2001 to 2003, coordinated by the Parasitology Institute of the Sichuan CDC, with the collaboration of international teams; the investigations, on 7138 subjects in the study area, included the detection of AE lesions in the liver using ultrasound examination, and serodiagnosis with *E. multilocularis*-specific Em18-blot, and answers to a questionnaire on the assumed socio-economical and behavioral risk factors such as age, gender, county of residence,

nationality (ethnic group), education level, number of dogs kept, dogs kept by neighbors, contact with fox skin products, drinking water sources, nomadic life style, income, livestock raising, habit of washing hands before eating, drinking non-boiled water, preventing flies from food and playing with dogs. The relationship between the disease prevalence and fenced area of pastures around winter settlements of the Tibetan herdsmen was calculated by using administration data on the "bundles of pens" distributed and sold to the household heads or group tenure heads by the commune authorities.

2) *Data from field investigations in 2003*, according to a strict sampling methodology, which included the burrow density of small mammals obtained by transect, used as an index of small mammal number, the measurement of the fenced areas in the winter pastures, answers to a questionnaire by herdsmen on socio-economical and behavioral (occupational) factors including pasture and livestock ownership, use of the fenced areas and grazing behaviors by households, and *E.multilocularis* infection in dogs through collecting and copro-PCR analyzing dog faces.

Our study revealed that the overall prevalence of AE was 3.1% (223/7,138); females (3.6%, 132/3,713) had a significantly higher prevalence than males [2.7%, 91/3,425, p=0.011, Odds Ratio (OR) = 1.440]. Herdsmen communities (5.2 %, 154/2,955) had higher prevalence than farmer communities (1.8%, 12/661) and urban populations (2.1%, 49/2,360). Multiple logistic stepwise regression analyses showed that AE prevalence increased with age in all three comparatively homogeneous populations of herdsmen, farmers and urban population. In the highly contaminated herdsmen communities, not preventing fly contact with food in households, which might be an indicator of hygiene behaviors, was associated with a higher probability of AE infection [$p<0.001$, OR=8.598]. In communities of farmers, the number of dogs kept ($p=0.022$, OR=1.722) and ownership of fox skin ($p=0.017$, OR=6.583) were found associated with AE infection. Both were more frequent in Shiqu than in Ganzi County and could partially account for prevalence differences between the counties. In urban populations, people using open streams as their drinking water source had a higher risk of AE than people using tap water and wells (tap water vs. stream, $p<0.001$, OR=0.276) and actively playing with dogs had a higher risk than persons who claimed never playing with dogs ($p<0.004$, OR=4.550).

Answers to questionnaires and field observations revealed that unlimited grazing by livestock was permitted in open pastures. On the contrast, the fenced pastures were well managed by timing of grazing and limiting livestock access. In comparison to fenced pastures (not overgrazed), the open pastures (overgrazed) had a higher density of small mammal burrows in valleys ($p=0.005$), valley entrances ($p=0.005$) and flatlands ($p<0.001$), as tested by non-parametric tests. Overgrazing seemed to be exacerbated by partial fencing of pastures, that promoted higher burrow density of small mammals in open, common, pastures: Spearman correlation analyses found that the larger fenced area, which indicated higher overgrazing pressure, led to higher burrow density of small mammal in the open pasture in all landscape types, namely valley (r_s=0.382, p<0.001), flatland (rs =0.312, p<0.001), piedmont (r_s=0.471, p<0.001) and valley entrance (r_s=0.296, p=0.001). The median burrow density of small mammals in open pastures was revealed to be independently associated with dog *E. multilocularis* infection (p=0.003, OR=1.048) by a multiple stepwise logistic regression analysis with consideration of dogs' sex and age as well as type of sampling. Partial fencing around the settlements in winter pasture was found to be significantly and independently associated with the risk of human alveolar echinococcosis in the surveyed villages (P=0.021) by a multiple stepwise logistic regression with consideration of age and gender.

Although overgrazing is an issue widely studied, yet the methodology for measuring overgrazing has not been well established. The relationship found between overgrazing and density of small mammals was either positive or negative, in different region, even in the same site. This phenomenon may partially be attributed to lack of proper definition and measurement of overgrazing. In our research, it was figured out that overgrazing did occur under two conditions based on socio-economical paradigm: 1) pastures are scarce resources in a community where livestock raising is a key industry; 2) the existence of communal pastures in the community. Furthermore, it was found that overgrazing also could be indirectly measured through measuring fenced pastures in Tibetan pastoralist settlements:

settlement with bigger fenced area has higher pressure of overgrazing in open pastures.

We also realized our weaknesses in the study which may ask for further researches with considering: 1) when transect is done, we should not only consider the current fencing situation; we also should collect data on timing of fencing, ownership of the fenced pastures and grazing behavior; 2) the overgrazing hypothesis holds satisfactorily for winter pastures; summer pastures should also be included into future research because summer pastures are all commons and their role in maintaining the parasitic cycle and/in transmission to humans cannot be ruled out; 3) future researches should also be associated with a quantitative direct assessment of small mammal species in the various habitants, which requires systematic trapping and identification in the same areas; 4) the study area is just a very small part of Tibetan Plateau, more researches in wider region are strongly needed to understand the extent of possible extrapolation of the overgrazing hypothesis.

From this research, we have major conclusions which are: 1) different communities may face different risk factors, which may include sex, age, residence, drinking water sources, playing with dogs and ownership of fox skin products; all seem to contribute in different ways to the transmission of *E.multilocularis* in the surveyed Tibetan communities. 2) an overall improvement of the hygiene situation and control of dogs' infection would be very important to limit AE/*E.multilocularis* transmission in Tibetan communities, and a community-specified control strategy would be more appropriate; 3) a socio-economical paradigm for measuring overgrazing was successfully developed and used for the first time in the Tibetan pastoralist communities; 4) overgrazing appears to increase the abundance of small mammals (mostly *Ochotona* spp), that may serve as reservoir hosts of the parasite, which may in turn promote maintenance and transmission of *E. multilocularis* in the Tibetan pastoralist communities. These observations represent a new example of the influence of occupational behaviors and property rights on ecological changes that may in turn favor the emergence of zoonotic diseases.

Introduction

Guiding questions: 1) What is the life cycle of Echinococcus (E.) multilocularis? 2) What is the disease "alveolar echinococcosis"? 3) What about the epidemiology situation of the disease in the world, in China and particular in Sichuan Tibetan communities? 4) What is the rationale to do this research?

Life cycle of *E.multilocularis* and the disease alveolar echinococcosis

Echinococcus multilocularis (*E.multilocularis*), the metacestode of the "fox tapeworm", is the pathogenic agent of alveolar echinococcosis (AE). *E.multilocularis* is a small tapeworm (1,2-4,5 mm in length) that infects definitive hosts which are always carnivores such as foxes, dogs and cats. In the definitive hosts the adult tapeworm, consisting of 2 to 6 proglottids, lives attached to the mucosa of the small intestine. The terminal proglottid contains mature eggs (ovoid, 30-40 µm in diameter). The embryonated eggs ("oncospheres"), the infectious stage, are long-lived and highly resistant to low temperature (down to -40℃), but easily destroyed over 50℃. The mature eggs are shed with definitive hose faeces and are spread in the environment. It is assumed that the intermediate host acquires the infections through ingestion of contaminated grass, fruits and vegetables. When the intermediate hosts (predominantly rodents or other small mammals) ingest eggs, the oncosphere hatches from the egg in the duodenum. The activated oncosphere penetrates the small intestine, enters blood vessels and reaches primarily the liver via the portal vein. In the liver the oncosphere proliferates into a metacestode consisting in an inner germinal membrane and an outer laminated layer. The fertile germinal membranes bud to form protoscolices which may subsequently develop into the adult stage in the definitive host. The lifecycle is thus completed when an intermediate host, carrier of viable protoscolices within the cysts, is devoured by a definite host (WHO/OIE manual, 2001).

When humans accidentally ingest the eggs, some may develop into a pseudo-tumor of parasitic origin and result in a particular parasitic disease, namely alveolar echinococcosis. The liver is the organ primarily affected; metastases are mainly observed in cases of advanced disease and may affect almost any organ; however extension to other organs than the liver does occur in 25% of cases at time of diagnosis (Kern et al., 2003). The disease either spreads via direct contact and invasion or via blood vessels. Secondary AE mostly affects the lungs and peritoneal cavity, but also brain, soft tissue, the spine and other bony structures. The disease is primarily characterized by an expansive and infiltrative growth in the liver, with obstruction of main vessels and bile ducts. Clinical features may be absent for many years and mostly become apparent in advanced disease. They may include hepatomegaly, jaundice, abdominal pain, weight loss, fever and manifestations of secondarily affected organs. In previous years AE was lethal within 10-15 years after diagnosis in 94-100% of untreated or inadequately treated human patients (Ammann and Eckert, 1996). New options for treatment of human AE have been developed. These options include improved surgical techniques and chemotherapy with albendazole or mebendazole. Although not fully satisfactory, chemotherapy is an option, predominantly in inoperable cases, and can be life saving, especially in patients with advanced AE (WHO/OIE, 2001, Eckert and Deplazes, 2004). Prognosis remains poor when diagnosed late, and/or when access to medical care is not available or difficult (Bresson-Hadni et al., 2000). Therefore, AE may be considered a serious public health problem in several regions including developed countries (Craig et al., 2003).

Human AE prevalence and *E.multilocularis* infection in animal host around the world

Due to the existence of very recently detailed reviews on this issue (Vuitton et al, 2003), this section will give a very brief outline of the situation around the world and China, while the situation in Sichuan Province will be given in more detail.

Geographically, AE is widely endemic in north hemisphere, including regions in central Europe, most of northern and central Europe, Asia and Parts of North America (Eckert et al., 2000). Endemic countries include Alaska and Central America, Canada, Armenia, Azerbaijan; Georgia, Iraq, Iran, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkey, Ukraine, Uzbekistan, China, Japan, Austria, Belgium, Czech Republic, Duchy of Luxembourg, France, Germany, Principality of Liechtenstein, Poland, Slovenia, Slovakia and Switzerland (Vuitton et al, 2003). Countries with isolated case reports are North India, Bosnia, Bulgaria, The Netherlands, Romania, Greece, Hungary, Croatia, Sweden, Denmark and Tunisia (Vuitton et al, 2003).

In Europe, Belgium, Czech Republic, Duchy of Luxembourg, Poland, Slovenia, Slovak Republic, and Greece were recently reported to have AE cases while France, Germany, Principality of Liechtenstein and Switzerland have been known to be endemic areas since the second part of 19^{th} century (Vuitton et al, 2003). A registry from January 1982 to December 2000, which covered 11 Europe countries including Austria, Belgium, France, Germany, Greece, Great Britain, Italy, Netherlands, Switzerland, Poland, the Czech Republic and Turkey, revealed that AE cases were autochthonous from Austria, Belgium, France, Germany, Poland, Switzerland and Turkey (Kern et al, 2003). The highest prevalence was recorded as 1/1000 (among 7,884 subjects) by sero-epidemiology screening in Eastern France (Bresson-Hadni et al, 1994). In western/central Europe, foxes were deemed as major definitive host (Raoul et al., 2001; Rausch, 1995; Vuitton, 2003); dogs and cats were also found to be infected by *E.multilocularis* (Gottstein, 2001). Arvicolid rodents, such as *Arvicola terrestri*s and *Microtus arvalis* were considered as main intermediate hosts (Giraudoux et al, 2002); Muskrats were also found infected with *E.multilocularis* (Rausch, 1995; Romig, 1999).

In North America, very high prevalence of AE in Eskimo communities in Alaska, especially on St Lawrence Island, in the northern part of the Bering Sea was observed between 1950 and 1990 (Rausch & Schiller, 1956; Wilson & Rausch, 1980; Stehr-Green et al., 1988). In this area, arctic foxes had an average infection rate of 77% and some 90% of these foxes preyed on northern voles, especially *Microtus oeconomus* considered to be the main intermediate host for *E.multilocularis*, as well as a species of lemming (*Dicrostonyx exsul*), the northern red-backed vole (*Clethrionomys rutilus*) and shrews (*Sorex cinereus*) (Rausch, Fay & Willianmson, 1990). Village dogs, found infected in 1951 with a prevalence of 12%, were also considered important in the spreading of the parasite close to human communities (Rausch & Fay, 2002).

In Asia part of former USSR, prevalence rates of 10/100000 or more were reported in Yukutia (Siberia), Chukot, Korjak autonomous districts, Kamchatka, Omsk and Tomsk regions and Altai territory (Bessonov 1998; 2002). In these parts of former USSR, nine species of carnivores (arctic fox, red fox, corsac fox, wolf, golden jackal, rural dog, raccoon dog, wild cat and domestic cat) have been found naturally infected, as well as 30 species of small mammals, including voles, mice, shrews, lemmings, marmots, jirds, muskrats, ground squirrels, jerboas, hares and hamsters (Bessonov, 1998). In Kazakhstan, larval stage of *E.multilocularis* was found in 18 species of rodents, including marmots, steppe marmot (*Marmota bobac*), grey marmot (*Marmota baibacina*), and gerbils, red-tailed gerbil (*Meriones libycus*) and great gerbil (*Rhomomys opimus*), especially in the forest-steppe, steppe zones and river valleys, and the adult stage in 4 species of definitive hosts, foxes(*Vulpes vulpes* and *V.corsac*), domestic dog (*Canis familiaris*), especially hunters' dogs, and wild cat (*Felis lybica*) (Shaikenov & Torgerson, 2002). In Middle East, presence of *E.multilocularis* in a fox in the north-west of Turkey, was reported by Merdivenci in 1965 (cited by Altintas, 1997). AE cases were also reported in Iraq and Iran (Rausch, 1995; Vuitton et al, 2003).

In Japan, a total of 383 human AE cases were detected since 1960s, up to 1999, and 5-9 cases per year are newly disclosed by the committee for Echinococcosis

Control in Hokkaido (Tsukada et al. 2000). In endemic areas of Japan including almost entire area of Hokkaido Island and Rebun Island, *E.multilocularis* circulates between foxes, stray dogs, and voles (Yamashita, 1973). *Clethrionomys rufocanus*, *C. rutilus* and *C. rex* have been identified as the main intermediate hosts involved in the cycle in nature (Takahashi et al., 1989; Takahashi & Nakata, 1995).

AE prevalence and *E.multilocularis* infection in China except for Sichuan Province

In China, there is a vast area being endemic with AE, which includes Inner Mongolia Autonomous Region, Helongjiang Province, Gansu Province, Ningxia Hui Autonomous, Qinghai Province, Tibet Autonomous Region, Xinjiang Uygur Autonomous Region, and Sichuan Province (Vuitton, et al, 2003) (See Figure IN-1).

In Heilongjiang Province, four human AE cases were documented in three counties of the province (Yu et al. 1994). Cases from Nahe County and Jamusi City were reported respectively (Li et al. 1985; Wen, 1990). These two cities are close to Da-xin-an-ling and Xiao-xin-anling mountains where deforestation and farmland extension were noted as early as the 1950s (Xia, 1996). No data are available on animal infection and the characteristics of the local cycle of the parasite are unknown.

Figure IN-1 Alveolar Echinococcosis Endemic Provinces and Autonomous Regions in China (According to Zhou HX, PhD thesis, 2001)

Legendary: AE is endemic in orange regions including Monglolia Autonomous Region, Helongjiang Province, Gansu Province, Ningxia Hui Autonomous, Qinghai Province, Tibet Autonomous Region, Xinjiang Uygur Autonomous Region, and Sichuan Province (Vuitton, et al, 2003)

In Inner Mongolia Autonomous Region, only 1 AE case was reported (Ji et al, 1987). One Corsac fox was found infected of *E.multilocularis* after examining 6 *Vulpes vulpes*, 9 *Canis lupus*, 28 dogs and 36 corsac foxes from 1998 to 1999, in Xinba'erhuyouqi (Tang et al., 2001). Two species of small mammals were found to be hosts of *E.multilocularis*, 2.4% (64/2635) for *M.brandti* and 16.7% (1/6) for *Meriones unguiculatus* (Xia, 1996).

Ningxia Hui Autonomous Region has been identified as an AE endemic area since 1965 (Mu, et al, 1991). In 1991, a mass screening using ultrasound and serological test revealed a prevalence of 5.9% (141/2389) in Xiji County, Guyuan Prefecture (Wang et al., 1991). A most recent ultrasound survey has confirmed the high prevalence found both in Han and Hui villages of this Autonomous Region (Yang et al., EID, in press). In the prefecture, both carnivores (*Vulpes vulpes*, dogs and cats) and small mammals (*Citellus dauricus*, *Myospalax fontanieri*) were found to harbor *E.multilocularis* (E.P.S.N.R, 1999; Li WX et al, 1985; Zhou HX, PhD thesis, 2001).

Gansu Province was found to be a new large focus of AE, where the prevalence of human AE was 4.1% (135/3331), as assessed by ultrasound combined with 5 serology tests in central China (Craig P. et al., 2000). Only dogs were reported naturally infected with *E.multilocularis* (10.17%, 6/59), even if wolf, red fox and corsac fox were found in the endemic area (Craig, 1992). Two rodent species dominated the intermediate stages of the deforestation gradient, *Microtus limnophilus* a vole, and *Cricetulus longicaudatus*, a hamster (Giraudoux, 1998). Laboratory studies have proved that *M. limnophilus* is susceptible with production of fertile cystic lesions (Zhou, 2001). However, no natural *E.multilocularis* infection among these small mammals was found in this region so far (Giraudoux, 1998; Giraudoux, 2003; Zhou HX, PhD thesis, 2001).

Qinghai Province was probably the first province to be found endemic for AE, since AE cases were reported in 1964 there (Liu and Qu, 1964). First mass screenings of AE in 1997 and 1998 revealed a 1.52% (19/1253) AE prevalence in Yushu County and 0.29% (3/1046) in Zeku County (Liu et al., 1998; Schantz, 1998). Two among 15 stray dogs and 3 among 99 foxes were found infected with *E.multilocularis* (Schantz, 1998; Wang et al, 1999). The presence of *E.multilocularis* in *Ochotona curzoniae* (up to 15/113) was found in Yushu and Chengduo counties, and *Lepus oiostolus* (1/8) in Huangnan Prefecture (Wang et al, 1999).

Xinjiang Uygur Autonomous Region was found to be an AE endemic area as early as 1956 and a cumulative report of 6 clinical cases was published in 1965 (Yao et al., 1965). It was reported that red foxes and wolves had *E.multilocularis* infection

(Wang et al., 1989; Watihan, 1987). Small mammals (*Mus musculus* and *Spermophilus erythirogenys*) were also found infected with *E.multilocularis*, but no protoscoleces were found in the cysts (Qi et al, 1995).

In Tibet Autonomous Region, human AE cases were reported from Changdu and Naqu Prefecture (Puzhi, 1999; Yixijacuo, 1992). In Naqu county, *E.multilocularis* infection was found to be 11.1% (2/18) in dogs and 8.7% (4/46) in *Ochotona curzoniae* (Qiu et al, 1995).

AE prevalence and *E.multilocularis* infection in Sichuan Province, China

Sichuan Province is located in the southwest part of China with an area of 485,000 km^2 and 83.6 millions inhabitants in 2003. Its population size ranks second in China with a share of 9.5% of the whole population of China. Most people reside in central and eastern part of the province, while only about 5.8 million, mostly minority ethnic groups, live in three autonomous prefectures which cover 297,600 thousand km^2 in western Sichuan Province, namely, Ganzi Tibetan Autonomous Prefecture, Aba Tibetan and Qiang Nationality Autonomous Prefecture, and Liangshan Yi Nationality Autonomous Prefecture (See Figure IN-2).

Western part of Sichuan Province is one of AE high endemic areas in China. Before 1997, AE cases were only reported by hospitals. In 1991, Liu et al reported 15

Figure IN-2 AE endemic areas in Sichuan Province

Note: 1) Lighter gray area including Ganzi Tibetan Autonomous Prefecture and Aba Tibetan and Qiang Autonomous Prefecture is the AE endemic region in Sichuan Province; 2) Shiqu County, far northwest part of Sichuan Province, is the survey area of the research.

AE cases that were all from Shiqu County, Ganzi Tibetan Autonomous Prefecture. Among them were 13 males and 2 females, aged 22 to 58 years old (Liu et al., 1991). Also in 1991, it was reported 35 cases of AE patients from Shiqu County, Dege County, Seda County, Ganzi County, Kangding County in Ganzi Tibetan Autonomous Prefecture and Ruo’ergai County in Aba Tibetan and Qiang Nationality Prefecture (Lin & Hong, 1991). Between 1984 and 1994, 24 cases of AE from Ganzi Tibetan Autonomous Prefecture were diagnosed and treated at Chongqing University of Medical Sciences; 10 cases were from Shiqu County, 5 cases from Ganzi County, 4 cases from Kangding County, 4 cases from Seda County and 1 case from Luohe County. The 24 cases had an average age of 44 years; only 5 were female and the longest illness time for some of these patients was 16 years (Yao et al, 1994). However, these numerations could overlap due to lack of systematic registration system for AE patients in the province, which means that a patient could be reported more than one time.

Since 1997, large-scale human AE screening began to be done in the Tibetan communities in Sichuan Province. Ganzi County and Shiqu County were selected to carry out the investigation that screened 3,999 people in 4 livestock raising-townships, 2 agriculture-townships and 2 urban communities. AE infection rate for the whole population was 1.90% (85/3999) (Qiu et al, 2000). AE infection rate was higher in herdsmen communities: 5.45% (44/809), compared with farmers (1.14%, 6/526) and the figure for the whole screened population (infection rate 1.90%, 85/3999) (Qiu et al, 2000).

Since 1983, systematic investigations of *E.multilocularis* infection in animals have been done in Ganzi County and Shiqu County. In 1983, natural *E.multilocularis* infection was found in the ileum of a stray dog in Ganzi County, which was claimed to be the first revelation of the existence of *E.multilocularis* in China (Zhu et al, 1983). In 1989, observation of fixed (10% formalin), dehydrated (ethanol) and colored (hematoxylin) worms in the intestine of 92 autopsied dogs from 1983 to 1986 were reported. In Ganzi County, 10/41 stray dogs and in Shiqu County 4/44 stray dogs had *E.multilocularis* infection. In addition, 7 owned dogs, 3 owned cats, 5 foxes and 1 wolf were examined and found without infection (Qiu et al, 1989). *Vulpes ferrialta* (Tibetan fox) was found with an infection rate of 44.4% (76/171) (He JG, et al, 2000).

From 1987 to 1988, black-lipped pikas (*Ochotona curzoniae*) were investigated to understand their potential role in *E.multilocularis* infection as intermediate host in Shiqu County. In 1987 autumn (November); 154 *Ochotona curzoniae* were examined and 4 were found with *E.multilocularis* infection (infection rate, 2.6%). In 1988 spring (May), 60 *Ochotona curzoniae* were examined and infection rate was 8.3% (5/60) (Qiu et al, 1989). In 1987, *E.multilocularis* infection was reported among yaks (6.2%, 6/97) and sheep (7.7%, 3/39) (Qiu et al, 1989). However, when these lesions were further tested by histological and molecular methods, it was revealed that those multilocular cysts visually deemed to be *E.multilocularis* were actually G1 strain of *E.granulosus* (Heath et al., 2004). Between 1997 and 1998, wild animals were captured and examined for *E.multilocularis* infection; *E.multilocularis* infection was 5.6% (13/233) in *Ochotona curzoniae*, 7.1% (1/14) in *Lepus oiostolus*, and 3/12 in *Pitymys irene*. No infection was found among 77 *Mus musculus* (He JG, et al, 2000).

The distribution of animal species naturally infected with *E.multilocularis* in P.R.China is shown in Table IN-1

Table IN-1 Animal species naturally infected with *E.multilocularis* in P.R.China (Zhou HX, PhD thesis, 2001)

<table>
<tr><th>Hosts</th><th colspan="3">Recorded species</th><th>Recorded provinces</th><th colspan="2">Infections/Sample size and prevalence</th><th>Sources</th></tr>
<tr><td rowspan="10">Definitive hosts</td><td rowspan="10">Canidae</td><td rowspan="6">Vulpes</td><td rowspan="3">V.vulpes</td><td>XUAR</td><td>11/36</td><td></td><td>Wang, 1989</td></tr>
<tr><td>SP</td><td>12/21</td><td></td><td>Qiu, 1998</td></tr>
<tr><td>NHAR</td><td>3/11</td><td></td><td>Li, 1985</td></tr>
<tr><td>V.corsac</td><td>IMAR</td><td>2/6</td><td></td><td>Tang, 1998</td></tr>
<tr><td rowspan="2">V.ferrilata</td><td>QP</td><td>3/9</td><td></td><td>Wang, 1999</td></tr>
<tr><td>SP</td><td>13/22</td><td></td><td>Qiu, 1998</td></tr>
<tr><td rowspan="4">Canis</td><td>C.lupus</td><td>XUAR</td><td>1/2</td><td></td><td>Wang, 1989</td></tr>
<tr><td rowspan="3">C.familiaris</td><td>GP</td><td>6/59</td><td>10.2%</td><td>Shi, 1995</td></tr>
<tr><td>QP</td><td>2/16</td><td></td><td>Wang, 1999</td></tr>
<tr><td>SP</td><td>40/242</td><td>16.7%</td><td>Qiu, 1998</td></tr>
<tr><td rowspan="11">Intermediate hosts</td><td rowspan="7">Rodentia</td><td rowspan="2">Arvicolinae</td><td>M.brandti</td><td>IMAR</td><td>64/2635</td><td>2.4%</td><td>Tang, 1988</td></tr>
<tr><td>M.irene</td><td>SP</td><td>3/12</td><td></td><td>Qiu, 1998</td></tr>
<tr><td>Gerbillinae</td><td>M.unguiculatus</td><td>IMAR</td><td>1/6</td><td></td><td>Tang, 1988</td></tr>
<tr><td>Cricetinae</td><td>M.fontanieri</td><td>NHAR</td><td>1/320</td><td>0.3%</td><td>Hong, 1987</td></tr>
<tr><td rowspan="2">Sciuridae</td><td>S.erythrogenys</td><td>XUAR</td><td>2/2211</td><td>0.1%</td><td>Qi, 1995</td></tr>
<tr><td>S.dauricus</td><td>NHAR</td><td>9/656</td><td>1.4%</td><td>Li, 1985</td></tr>
<tr><td>Muridae</td><td>M.musculus</td><td>XUAR</td><td>1/7147</td><td>0.0%</td><td>Qi, 1998</td></tr>
<tr><td rowspan="4">Lagomorpha</td><td rowspan="2">Ochotonidae</td><td rowspan="2">O.curzoniae</td><td>QP</td><td>11/319</td><td>3.5%</td><td>Wang, 1998</td></tr>
<tr><td>SP</td><td>41/607</td><td>6.8%</td><td>Qiu, 1998</td></tr>
<tr><td rowspan="2">Leporidae</td><td rowspan="2">L.oiostolus</td><td>SP</td><td>6/89</td><td>6.7%</td><td>Qiu, 1998</td></tr>
<tr><td>QP</td><td>1/8</td><td></td><td>Wang, 1998</td></tr>
</table>

GP:Gansu Province; IMAR: Inner Mongolia Autonomous Region; TAR: Tibet Autonomous Region; Qinghai: Qinghai Province; NHAR: Ningxia Hui Autonomous Region; SP: Sichuan Province; XUAR: Xinjiang Uygur Autonomous Region

Research rationale and aim

The available data in animal hosts of *E.multilocularis* thus show that the transmission cycle of *E.multilocularis* functions very well in the Tibetan communities and is the source of a significant number of human infections. It is known that small mammals are intermediate hosts of *E.multilocularis* and in other studies performed in various geographical locations such as eastern France and Gansu Province, China, a positive relationship was revealed between density of small mammals and *E.multilocularis* transmission (Giraudoux et al., 1997; 2000).

During field visits in 2001 and 2002, simple visual observation of the pastures (Figure IN-3, 4, 5, 6, 7) showed that the small mammals were extremely abundant: high density of small mammals could thus also be a key reason underlying the high prevalence of human AE. The reasons for the abundance of small mammals were however unknown and their understanding should be an important issue for understanding the particular location of the disease in Sichuan Province, and guide potential control measures. Through field observation (Figure IN-3, 4, 5, 6, 7), we assumed that grazing practice could influence the population of small mammals; in particular, overgrazing could have a major influence in promoting higher density of small mammals. Until now, very few researches have tried to hunting down the

Visual difference between fenced pastures and open pastures

Figure IN-3 Black Lipped Pika on the Tibetan plateau (*Ochotona curzoniae*)

Figure IN-4 Fenced Pasture (Yellow) and Open Pasture (Red)

Figure IN-5 Fenced Pasture (yellow) and Open Pasture (brown and almost bare)

Figure IN-6 Fenced pasture

Figure IN-7 Open pasture with burrows of small mammal

Figure IN-8 A young yak inside a fenced pasture

reasons underlying the high prevalence of AE in the communities from the socio-economical perspective. Therefore, the aim of the research was to explore and better understand the impact of socio-economical factors, in particular human behavior leading to overgrazing, on the transmission of AE/*E.multilocularis*, with an approach integrating socio-economical and ecological methodologies. The detailed socio-economical and ecological background will be put forward in Chapter 1, Chapter 2, and Chapter 3.

In summary: AE/E.multilocularis is a major public concern globally; the prevalence in China is quite high, in particular Tibetan pastoralist communities; the reasons behind the high AE epidemiology in Tibetan pastoralist communities are however unknown; socio-economical and ecological aspects, particularly grazing practice, were assumed to be possible reasons and were suggested to be examined by the research.

Chapter 1 Geographic, demographic, climatic, socio-economical and behavioral particularities of Sichuan Province, PR China, and their relationship with the epidemiology of alveolar echinococcosis (AE)

Guiding questions: 1) What are the backgrounds in terms of geography, demography, climate of the Tibetan plateau areas, and in terms of socio-economics and behavior of Tibetan communities, in Sichuan Province? 2) What are the socio-economical and behavioral risk factors for AE transmission in the Tibetan communities?

1.1 Geography, demography and climate of Sichuan province, PR China

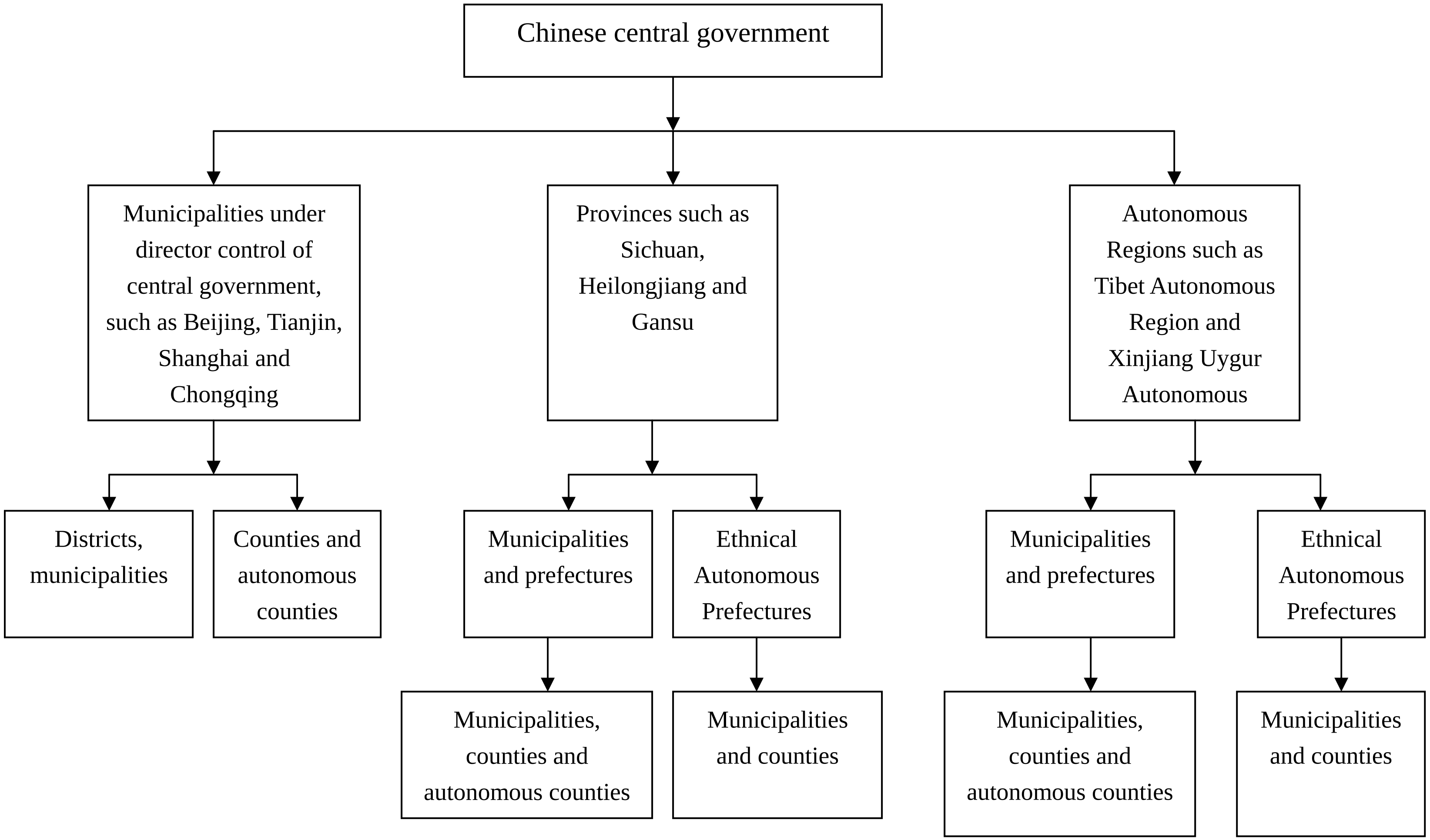
In Sichuan Province, AE is endemic in Aba and Ganzi prefectures where the population is comprised mostly by Tibetan people (See Figure IN-2).

The Autonomous Prefecture of Aba Tibetan and Qiang Nationality is located in the southeast edge of Qinghai-Tibet Plateau, northwest part of Sichuan Province (See Figure IN-2). It neighbors Chengdu Plain in the southeast and Qinghai Province and Gansu Province in the north as well. It covers an area of 84.2 thousand km^2 with 13 counties under its jurisdiction, namely Ma'erkang, Jingchuan, Xiaojing, Aba, Rou'ergai, Hongyuan, Rangtang, Wenchuan, Lixian, Mengxian, Songpan, Jiu Zaigou and Heshui. By the end of 2003, there were 847 thousand inhabitants and among them

Tibetan were 52.3%, Qiang nationality 17.7%, Hui nationality (Islamic population) 3.2%, Han Nationality 26.6%, other nationalities 0.2%. The landscape of Aba Prefecture features with plateau and valley. In the southeast part of the prefecture, the landscape is mainly high mountain valley; in the middle part of the prefecture it features with altitude plain and in the northwest part it features with plateau. Two branch rivers of Yangtze River (Changjiang River), namely Mingjiang river and Daduhe river cut across the prefecture. Yellow River (Huanghe River) also passes the prefecture in the north. The temperature decreases from southeast to northwest with increasing altitude. Northwest part of the prefecture has a longer winter and a yearly average temperature from 0.8°C to 4.3°C. In southeast part, it has a comparatively higher yearly temperature 5.6°C to 8.9°C. In high mountain and valley areas, the climate changes in a vertical way from subtropical zone, temperate zone, cool temperate zone, to frigid zone (Prefecture Government, Aba Tibetan and Qiang Nationality Autonomous Prefecture, 2003).

Ganzi Prefecture is located in the western part of Sichuan Province (See Figure IN-2). It borders Aba Prefecture and Ya'an in the east, Liangshan Prefecture in the south, Aba prefectureChangdu District of Tibet in the west, Yushu and Guoluo prefectures of Qinghai in the north. It had a population of 900, 000 by the end of 2003 and Tibetan accounted for 78.4%, Han for 18.9%, Yi for 2.2%, and Hui (Muslim) and others for 0.5%. The area of the prefecture is 153 thousand km^2, which is the biggest one among administrative areas of the same level in the province (See Figure I-1, Chinese administrative region institutional structures), accounting for 1/3 of the area of Sichuan Province. It has jurisdiction over 18 counties that cover 325 townships. It features with continent monsoon plateau climate. Yearly average temperature is 7.8℃. The average altitude is 3500 meter. The landscape may be that could be categorized into high mountain, peak plain altitude plain, and high mountain valley. The average altitude is 3500 meter. Yearly average temperature is 7.8℃ (Prefecture Government, Ganzi Tibetan Autonomous Prefecture, 2003).

Figure I-1 Chinese Administrative Region Institutional Structures



1.2 Socio-economical and behavioral characteristics of the Tibetan communities

In western Sichuan Province, Tibetan communities can be roughly divided into agriculture communities and herdsmen communities.

Agriculture communities are usually located in valleys below an altitude of 3500 meter, where temperature is warm and rainfall is enough for agriculture production. The major agriculture product is barley in these agriculture communities and barley is usually fried and milled into powder to make Zhanba (or Tsampa), a kind of food that is a mixture of barley powder, water (or tea), sometimes with Tibetan yak butter and sugar. Zhanba is also the main food of herdsmen communities, and the mixture is usually prepared using bare fingers and hand by every consumer.

Herdsmen communities are usually scattered in areas above an altitude of 3500 meters, where livestock raising is the key industry. The livestock is comprised mostly of yaks, sheep, goats, horses, and a small number of pigs (Shiqu County Editorial Committee for Shiqu County Record, 2000; Rangtang County Editorial Committee for Ganzi County Record, 1997; Hongyuan County Editorial Committee for Hongyuan County Record, 1996; Ruo’ergai County Editorial Committee for Ruo’ergai County Record, 1996).

In the Tibetan communities, the main religion is Tibetan Buddhism, which has several different branches in the region. For example in Shiqu County, there are 5 branches of Tibetan Buddhism including Benbo, Ningma, Shajia, Gelu, and Geju (Shiqu County Editorial Commission for Shiqu County Record, 1997). However, there are also small numbers of Muslims and Christian populations in these communities. Because the main religion is Buddhism that forbids animal killing, local Tibetans seldom slaughter livestock by themselves. Hui (Muslim) people are usually invited to do the job (Shiqu County Editorial Committee for Shiqu County Record, 2000; Rangtang County Editorial Committee for Ganzi County Record, 1997; Hongyuan County Editorial Committee for Hongyuan County Record, 1996; Ruo'ergai County Editorial Committee for Ruo'ergai County Record, 1996). It is normally that around 5% of livestock are slaughtered for meat or sale; milk, skin, and fur are also major products; milk is almost totally self-consuming in the forms of direct drinking, milk tea, yogurt, dried yak cheese and yak butter; dried yak cheese and yak butter could be sold in the market. Traditionally, it is believed that the more yaks (livestock), the richer. Yak number is more important than yak health (Shiqu County Editorial Committee for Shiqu County Record, 2000; Rangtang County Editorial Committee for Ganzi County Record, 1997; Hongyuan County Editorial

Committee for Hongyuan County Record, 1996; Ruo’ergai County Editorial Committee for Ruo’ergai County Record, 1996).

The Tibetans refuse to kill any other lives and even try and help weakened animals due to their believing in Buddhism. For example, there are large numbers of stray dogs around temples in herdsmen communities; the Lamas (Buddhist priests/monks) always feed and protect them. Usually, in herdsmen communities there is at least one temple per township, which leads to quite a big number of stray dogs existing in the communities. Also, when herdsmen have too many dogs, they always bring the dogs to a town or a temple where food is easier to find. There is no special agency responsible for controlling stray dogs, and all dogs are beyond the care of local veterinarians in these communities.

In herdsmen communities, semi-nomadic life is a thousand years of tradition. They usually move to different pastures seasonally. In winter, they stay in winter pastures where some of them may have houses while others live in tents. From spring to autumn, they stay in summer pastures and some of them may also have access to spring or autumn pastures if these pastures are designated as spring or autumn pastures. Usually, the winter pastures are located in comparatively lower altitude areas, where temperature is higher in winter and the traffic is more convenient, while summer pastures are located in valley ends or other higher altitude areas (Shiqu County Editorial Committee for Shiqu County Record, 2000; Rangtang County Editorial Committee for Ganzi County Record, 1997; Hongyuan County Editorial Committee for Hongyuan County Record, 1996; Ruo'ergai County Editorial Committee for Ruo'ergai County Record, 1996).

Herdsmen of a same tribe usually form a village or a township. The pastures in winter areas are comparatively accurately assigned to group of herdsmen (Shiqu County Editorial Committee for Shiqu County Record, 2000; Rangtang County Editorial Committee for Ganzi County Record, 1997; Hongyuan County Editorial Committee for Hongyuan County Record, 1996; Ruo'ergai County Editorial Committee for Ruo'ergai County Record, 1996). Use of summer pastures by herdsmen is still under the management of township government, which is quite similar to the traditional way of pasture management. In early spring of year 2002, in Yiniu Township, Shiqu County, we observed that the local government distributed summer pastures to herdsmen; they also gave the order to herdsmen to move from winter pastures to summer pastures to preserve grass for winter grazing in the winter pastures. Some herdsmen also cut grass and store the hay on the roof of houses for wintertime grazing.

There is a distinct division of labor in Tibetan herdsmen families. Male herders are mainly responsible for business outside families (shopping and trade), organization of moving around the pastures and sometimes care of livestock. Female herders are responsible for taking care of livestock, milking livestock and, preparing yak faeces cakes (See Figure I-2, 3, 4, 5) to be fuel usually immediately after milking and with bare hands, feeding dogs and doing other family works, especially cooking (Shiqu County Editorial Committee for Shiqu County Record, 2000; Rangtang County Editorial Committee for Ganzi County Record, 1997; Hongyuan County Editorial Committee for Hongyuan County Record, 1996; Ruo'ergai County Editorial Committee for Ruo'ergai County Record, 1996).

To keep some dogs is a must for herdsmen to protect their properties including houses, tents, and livestock. In the Tibetan herdsmen communities, the density of population is very low, for example, in Shiqu County there are only 2.47 persons per km^2 (Shiqu County Editorial Committee for Shiqu County Record, 2000). Therefore, for security reason they need dogs. There are some wild animals in the area, for example wolves and bears, and even stray dogs, which also impose threat to livestock. Owned dogs are usually tied to a stick fixed on the ground in daytime on the doorway of houses or tents (See Figure I-6). At night, they are released so that they can roam around to find and attack possible aggressors and give early alert. Livestock is also kept around houses or tents at night. These dogs, especially strong dogs, usually follow herders to move among pastures. Dogs were observed to search small mammals during our field visits (See Figure 7). Dogs' faeces are widely distributed around rooms, may pollute the yak faeces and the human micro-environment and consequently increase the opportunity contact between human and dog faeces (See Figure I-8, 9, 10, 11 and 12).

In summary for literature review: It seems that demographic situation, livestock raising industry and Buddhism practice make the pastoralist Tibetan communities to be suitable of the existence of big number of owned dogs and stray dogs, which are important definitive hosts of E.multilocularis; However, researches concerning how these socio-economical and behavioral influence the human AE prevalence are few; Therefore, we try to address the issue by doing a risk factors research.

Environment and Behaviors of Pastoral Tibetans (1)

Figure I-2 Hill of yak faeces in the open air

Figure I-3 A girl collecting yak faeces

Figure I-4 Yak faeces piled inside a tent

Figure I-5 Entering yak faeces with bare hands

Figure I-6 Tibetan dog-the main AE/E. multilocularis transmission source?

Environment and Behaviors of Pastoral Tibetans (2)

Figure I-7 A dog presumably searching small mammals

Figure I-8 Dog faeces contaminating environment

Figure I-9 Stray dogs in front of a Buddhism temple

Figure I-10 A young man trying to drive out Pikas with cigarette smoke

Figure I-11 Preparing and eating "zhanba" with bare hands

Figure I-12 Placing a bowl beside a hill of yak faeces (lower right)

1.3 Risk factors of human AE transmission in the Tibetan communities.

Qian Wang, Dominique A. Vuitton, Qiu Jiamin, Wen Yang, Peter M. Schantz, Francis Raoul, Philip S. Craig, Patrick Giraudoux.

Socio-economical and Behavioral Risk factors of Alveolar Echinococcocosis in Tibetan Communities, Sichuan Province, China. ***Submitted to the "American Journal of Tropical Diseases and Hygiene".***

Abstract

Introduction

Materials and methods

Results

Discussion

Acknowledgements

References

In summary for the paper: 1) The community of herdsmen was found to be at the highest risk for alveolar echinococcosis in the studied area; the risk increased with age in all studied communities. 2) "Owning dogs" and "playing with dogs" were identified as significant risk factors for the transmission of **E. multilocularis** ***to humans in farming and urban communities respectively. 2) Other risk factors for*** **E. multilocularis** ***transmission to humans included "not preventing flies from food contact" in herdsmen communities, "county of residence (Shiqu county)" and "ownership of fox skin" in farmers' communities, as well as "female gender" and "drinking stream water sources" in urban communities.***

Socio-economical and Behavioral Risk factors of Alveolar Echinococcocosis in Tibetan Communities, Sichuan Province, China

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Abstract

Data from two cross-sectional abdominal ultrasound investigations on 7,138 subjects were used to understand the mode of alveolar echinococcosis (AE) transmission, infection by larval stage *E.multilocularis,* and explore opportunities for prevention in communities of the Sichuan part of Tibetan plateau, Shiqu County and Ganzi County, PR, China. The overall prevalence of AE was 3.1% (223/7,138); females (3.6%, 132/3,713) had a significantly higher prevalence than males (2.7%, 91/3,425, p=0.011, OR=1.440). Herdsmen communities (5.2 %, 154/2,955) had higher prevalence than farmer communities (1.8%, 12/661) and urban populations (2.1%, 49/2,360). Risk factors analyzed included age, gender, county of residence, nationality, education, number of dogs kept, dogs kept by neighbors, contact with fox skin products, drinking water sources, nomadic life style, income, livestock raising, habit of washing hands before eating, drinking non-boiled water, preventing fly from food and playing with dogs. Multiple logistic stepwise regression analyses showed that AE prevalence increased with age in all three comparatively homogeneous populations of herdsmen, farmers and urban population. In the highly contaminated herdsmen communities, not preventing fly from food in households, which might be an indicator of hygiene behaviors, was associated with a higher probability of AE infection [p<0.001, Odd Ratio (OR)=8.598]. In communities of farmers, the number of dogs kept (p=0.022, OR=1.722) and ownership of fox skin (p=0.017, OR=6.583) were found associated with AE infection. Both were more frequent in Shiqu than in

Ganzi county and could partially account for prevalence differences between the counties. In urban populations, people using open streams as their drinking water source had a higher risk of AE than people using tap water and wells (tap water vs. stream, $p<0.001$, OR=0.276) and actively playing with dogs had a higher risk than persons who claimed never playing with dogs ($p<0.004$, OR=4.550). These results confirm that the Tibetan plateau in Sichuan province is a highly endemic area of AE and that risk factors may vary according to structure and practices of communities; consequently, control strategies should also vary accordingly.

Key words: alveolar echinococcosis, *Echinococcus multilocularis,* behavior, socio-economics, risk factors, Tibetan communities, dog, gender issue

Introduction

Alveolar echinococcosis (AE), caused by the metacestode of the "fox tapeworm" *Echinococcus (E.) multilocularis*, is considered to be one of the most pathogenic and chronic parasitic zoonoses in temperate and arctic regions of the Northern Hemisphere (Eckert and Deplazes, 1999; 2004). AE is a major public health problem in western China (Vuitton, et al, 2003; Wen, et al., 2002). In Sichuan province, China, AE mostly affects the Tibetan communities (Qiu et al., 1999). In the pastoral areas of affected Tibetan communities, *E.multilocularis* larval infection was recorded in 25% (3/12) of plateau voles (*Microtus irene*) and in small lagomorphs [6.7% (5/75) of the black-lipped pika (*Ochotona curzoniae*) and 7.1% (1/14) of Tibetan hares (*Lepus oiostolus*)] (Qiu et al., 1999). Overgrazing of the pastures was suggested to be a key factor promoting abundance of small mammals which may in turn promote AE transmission (Wang, et al., 2004). However, few control measures have been implemented, partly due to the lack of knowledge in the actual risk factors of AE infection in this particular area.

In Tibetan communities, the population can be separated into herdsmen, farmers, and urban population in terms of their living place and occupational practice. The situation, regarding environment and behavior is very different for these three populations as well as they may be in the various districts (counties) where Tibetan communities live. We thus addressed the epidemiology characteristics and especially the specific risk factors for each population in two counties of the Sichuan Tibetan plateau in order to better understand the mode of transmission of *E. multilocularis* in this area which is also endemic for *E. granulosus* infection (Wang et al, 2001), and to identify specific control opportunities for these populations separately.

Materials and methods

Description of the study area

Surveys were conducted in two counties, Ganzi County and Shiqu County, Ganzi Tibetan Autonomous Prefecture, Sichuan, China in 1997, 2001, 2002 and 2003. The two counties are located at 97°20”-100° 25”E and 36° 19”-31° 24”N. They share a border with Qinghai Province in the east, north and west and with the Tibet Autonomous Region in the south. Shiqu County covers an area of 25,100km^2, with a mean elevation of 4,200m. Grassland covers an area of 21,000 km^2 of which 19,000 km^2 can be used as grazing pasture. By the end of 1997, there was an estimated livestock population of 581,470 mainly consisting of yak, sheep, goat, horse and small number of pigs. The human population of this county was approximately 63,400 and 96.8% were ethnic Tibetans. There were 49,100 herdsman representing 77.6% of the population. Ganzi County covers 7,350 km^2 with a mean elevation of 3,410 m. Grassland covers an area of 5,370 km^2. By the end of 1997, there was an estimated livestock population of 326,730 of the same species as in Shiqu county. The human population was 55,550 and 95% were Tibetan. There were 19,000 herdsmen. The weather of both counties is affected by plateau monsoon climate. Winter is longer than summer and there is no day absolutely free of frost. The humid season stretches from May to October. The yearly rainfall ranges from 460 mm to 636 mm. The average temperature is -10℃.

Data collection

Township officials and village cadres passed messages through herdsmen to inform the inhabitants where they could get free medical examination for echinococcosis. Thus, volunteer, self-selected subjects went to one of the designated screening places. Before examination, informed consent was obtained from all adult subjects and from the parents of minors. The studies were approved by the Ethical Committee of Sichuan Institute of Parasitic Diseases, Sichuan Province as well as those of collaborating investigators, according to the regulation operating for the NIH of the USA. After answering an epidemiological questionnaire, each registered person was given an abdominal examination using a portable ultrasound machine. For people found to have AE lesions in their liver or suspect AE, 5 mL of blood was taken for serodiagnosis which was performed using *E. multilocularis*-specific Em18-blot (Ito et al., 1993). Diagnosis was based on the ultrasound characteristics as recommended by the WHO-Informal Working Group Echinococcosis Ultrasound Classification Network and used in previous mass screenings in PR China (Bartholomot et al, 2002). From the epidemiological questionnaires, among potential transmission risk factors, age, gender, county of residence, nationality (ethnic group), education level, number of dogs kept, dogs kept by neighbors, contact with fox skin products, drinking water sources, nomadic life style, income, livestock raising, habit of washing hands before eating, drinking non-boiled water, preventing flies from food and playing with dogs were analyzed.

Statistical analyses

Statistical analysis included a general description and analyses of the age and gender structure as well as AE prevalence of the population under study, globally and in each of the studied counties. A sex stratified stepwise logistic regression taking age factor into account was then used to characterize AE prevalence differences among farmers, herdsmen and urban populations. Finally, single factor and multiple factor stepwise logistic regressions were employed to identify risk factors fo each of the three populations. Factors with P values less than 0.15 were kept for variable inclusion in multiple logistic regressions. Age had a 1-year increment and number of dogs had 1 dog increment. All these analyses used SPSS 10 software.

Results

A total of 7,138 subjects were screened in the 2 counties of the study and used for the analysis; 86.4% (6167/7,138) of the investigated population were Tibetans. Those subjects who listed occupations as "farmers" and "herdsmen" were all Tibetans. In the analyses, all patients identified in previous surveys or diagnosed in hospitals were not included. Herdsmen communities had 2,955 subjects screened, farming communities 661, urban communities 2,360 and 1,043 subjects (mostly under 15 years-old) were students. The average age of the population was 31.1 yrs (N=7,138, SD=16.4); the average age of males 31.0 (N=3,425, SD=16.5) and the average age of females 31.2 (N=3,713, SD=16.3). The average number of dogs kept was 1.17 (SD=1.13) by the adult population, and 1.44 (SD=1.16), 1.04 (SD=0.95), as well as 0.88 (SD=1.05) for herdsmen, farmers and urban communities respectively.

1. AE prevalence according to gender and age.

The overall AE prevalence for the population was 3.1% (223/7138) in which prevalence in males was 2.7% (91/3425) and prevalence in females was 3.6% (132/3713). There was a tendency of increasing prevalence with age in all groups except for students (See table 1). Overall prevalence in herdsmen was 5.2 % (154/2955), 4.8 % in males (65/1368) and 5.6 % in females (89/1587). Overall prevalence in farmers was 1.8% (12/661), 1.1% in males (3/268) and 2.3% in females (9/393). In urban population prevalence was 2.1% (49/2360), 1.3% in males (16/1235) and 2.9% in females (33/1125). In students prevalence was 0.3% (3/1043), 0.4% in males (2/483) and 0.2% in females (1/560).

Multiple stepwise logistic regression which included age, gender and community factors (urban community, rural community, herdsmen community), showed that prevalence in females was significantly higher than in males [p=0.011, Odd Ratio (OR) =1.440)]. Using stratified logistic regression in which gender was the stratifying factor and included age and community, the herdsmen community was identified as the population with the highest AE prevalence (See table 2.)

2. Risk factors for herdsmen, farmers and urban communities.

For herdsmen communities, single factor logistic regressions found that county of residence (Shiqu vs. Ganzi, p=0.042, OR=1.788), age (p<0.001, OR=1.041), school education level (primary school vs. no education, p=0.020, OR=0.504; middle school vs. no education, p=0.002, OR=0.109), drinking water sources (well vs. stream, p=0.001, OR=0.331), income (above 10,000 RMB Yuan vs. less than 2,000 RMB

Yuan, p=0.012, OR=0.083), raising livestock (raising vs. not raising, p=0.044, OR=1.637), washing hands before eating (always vs. not, p=0.011, OR=0.484; sometimes vs. not, p=0.003, OR=0.333), drinking unboiled water (always vs. not, p=0.044, OR=0.657), preventing flies from food (preventing vs. not, p<0.001, OR=9.685) and playing with dogs (always vs. not, p=0.008, OR=2.977; sometimes vs. not, p=0.003, OR=3.262) were statistically significant risk factors. After multiple factors stepwise logistic regression analysis, only age (p<0.001, OR=1.036) and preventing flies from food (not preventing vs. preventing, P<0.001, OR=8.598) were found to be statistically significant (See table 3).

For farmers' communities, age (p<0.001, OR=1.076), number of dogs kept (p=0.024, OR=1.636), fox skin ownership (ownership except for hunting vs. no ownership, p=0.017, OR=6.389), and drinking unboiled water (always vs. not, p=0.040, OR=0.248) were statistically significant risk factors in single factor logistic regressions. After multiple factors stepwise logistic regression, only county of residence (Shiqu County vs. Ganzi County, p=0.009, OR=5.167) and age (p=0.001, OR=1.078) were found to be statistically significant risk factors. However, when the county of residence was not included in the analysis, the number of dogs kept was found to be statistically significant by forward stepwise multiple logistic regression (p=0.022, OR=1.722) and ownership of fox skin was found to be a statistically significant risk factor by backward stepwise multiple logistic regression (ownership of fox skin products through buying or donation vs. no ownership, p=0.017, OR=6.583) (See table 4). In fact, Shiqu County farmers owned more fox skin products (p<0.001) and kept more dogs than those living in Ganzi County (p<0.001). Therefore, co linearity might exist between county of residence and fox skin products ownership as well as between county of residence and number of dogs kept.

For urban population, single factor logistic regressions showed that county of residence (Shiqu vs. Ganzi, p<0.001, OR=3.516), gender, (female vs. male, p=0.007, OR=2.302) ethnic group (Tibetan vs. Han, p=0.003, OR=5.853), school education level (Primary school, middle school, college and above vs. no education respectively, p=0.031, <0.001, and 0.045, OR=0.348, 0.231, and 0.130 respectively), number of dogs kept (p<0.001, OR=1.429), fox skin ownership (ownership except for hunting vs. no ownership, p=0.025, OR=2.124), drinking water sources (well and tap vs. stream, p=0.008 and <0.001, OR=0.283 and 0.153 respectively), income (2000 ≤ Income<5,000 vs. Income<2,000 Yuan, p=0.008, OR=0.329), raising livestock (raising vs. not raising, p<0.001, OR=3.027) washing hands before eating (always and sometimes vs. never, p<0.001 and =0.031, OR=0.234 and 0.460), preventing flies from food (preventing vs. not, p<0.001, OR=2.984) and playing with dogs (always and sometimes vs. never, p<0.001 and <0.001, OR=6.943 and 4.222) were statistically significant risk factors. After multiple factors stepwise logistic regression, gender (female *vs.* male, p=0.009, OR=2.345), age (p=0.001, OR=1.031), drinking water sources (tap water *vs.* stream, p<0.001, OR=3.743; well *vs.* stream, p=0.033, odds ratio=0.354) and playing with dogs (always *vs.* never, p<0.004, OR=4.550; occasionally *vs.* never, p=0.024, OR=2.826) were statistically significant risk factors (See table 5).

Discussion

This study, which comprised more than 7,000 subjects screened for AE and thus constitutes the largest study of AE risk factors in a human community, assessed demography, occupation, environment, style of life, mode of production, and behavior in three populations, namely, herdsmen, farmers and urban populations of 2 counties of the Tibetan plateau in Sichuan Province, China. The study confirmed in this Tibetan area that herdsmen and females were at highest risk for AE, and showed that differences in prevalence among counties might be due to behavioral factors in addition to the well recognized environmental factors which determine *E. multilocularis* infection in intermediate and definitive animal hosts.

Herdsmen on the Tibetan plateau are definitely at high risk of *E. multilocularis* infection. AE prevalence in herdsmen was found as high as 8.5% in another study (Wang et al., 2004). A previous study showed that in livestock raising population (including farmers and herdsmen), playing with dogs and being a female were significant risk factors (Wang et al., 2001); other contacts with dogs were also pointed out (Schantz et al, 2003). Local Buddhist practices often result in large numbers of stray dogs in villages and this was suggested to be a possible factor of transmission promotion (Wang et al., 2001). In studies of animal infection in the Tibetan pasturing area, adult tapeworm infection of *E. multilocularis* was found in 44.4% (76/171) of Tibetan foxes (*Vulpes ferrilata*) and in 12.1-25.0% (4/33-5/20) of stray dogs (Qiu et al., 1999). Subsequently, a more systematic study in Shiqu County showed that 12% (44/371) of owned dogs were infected with *E. multilocularis* (Budke et al., 2005). Our field observations found that the environment, especially in the immediate area surrounding herdsmen houses, was highly contaminated by dog feces. Dogs are cared for by women of the community, and this could be a part of the explanation for the higher risk found in women. Such a higher risk in adult females was also found in rural communities of Gansu province, where dogs are also considered to be the main definitive host in contact with local populations (Craig et al, 2000). Additional risks for Tibetan women could also be related to the specific use of "yak feces cakes" as the main fuel in the herdsmen communities. The screened women reported that they could touch dog feces directly by doing this work and also mentioned that dogs sometimes defecated directly on the pile of yak feces. Entering yak feces into the stove, which usually is the work of women, could also result in contact with dog feces, and/or contaminating parasitic eggs, directly. In Shiqu County city, urban people also use "yak feces cakes" as fuel and the closer contacts with parasitic eggs could also apply to females in urban communities where differences according to gender were also found. However, a role for a certain degree of immune suppression during pregnancy cannot be ruled out: aggravation of previously stable AE during or immediately after pregnancy has been reported by the clinicians in charge of the follow-up of AE patients (Bresson-Hadni et al 1999), and recently, such a deleterious effect of pregnancy with occurrence of brain metastasis in a Chinese women in Ningxia has been observed (Yang et al, personal communication, manuscript under submission for publication). Both environmental/behavioral and immunological explanations fit with the observation of sex ratio in favor to females occurring only in adult cases, in our study and in Gansu Province (Craig et al, 2000; Bartholomot et al, 2002). Increased risk with age, in both genders, has been found in all epidemiological studies dealing with AE and is mainly explained by the long latent period of infection which may delay the diagnosis of the disease during several years, and even decades, after contamination (Vuitton et al, 2003).

In herdsmen communities, dogs are used to watch houses and tents and to drive wolves away at night. During the day, older dogs are usually tied to the doorway of tents or houses and younger dogs roam around inside and outside houses and tents. Dogs are released at night to protect livestock that are tied around the tents or houses. In these herdsmen communities, in terms of hygiene behavior, however, only preventing flies from from food was found to be a statistically significant protection against the disease; other assumed important factors such as keeping dogs, playing with dogs, owning fox skin products, water sources, washing hands or not before eating etc. were not statistically significant. The possible reason might be that the environment was so highly contaminated that only hygiene behavior related to direct food contamination could make a difference. We found significant differences depending on water source and dog owning in urban populations, whose direct environment, style of life and behavior are much more diverse, and this observation supports our hypothesis. Our household visits revealed that herdsmen families having the habit of preventing fly from food also had other types of behavior to improve the hygienic status in the houses. For example, in such families, food was stored in cupboards that not only prevent flies but also dogs to get in contact with the food; in fact, we also observed that young dogs were permitted to get access into places where food was stored in some households. However, other reasonable combinations of variables might be significant as well, and the "fly" factor may be a surrogate for some causal variables undetected at present, or even, more directly, transport of *E. multilocularis* eggs by flies. Until now, only *E. granulosus* eggs were convincingly shown to be transported by flies (Lawson and Gemmell, 1985), but nothing is known about this mode of contamination of food regarding *E. multilocularis*.

In the communities of farmers, farmers in Shiqu County had a higher risk of AE than farmers in Ganzi County. Our analyses suggested that the difference may lie both in the ownership of fox skin and in number of dogs kept; the people who kept several dogs or owned fox skin products, had higher risk of AE infection. There was co-linearity between the county of residence and the number of dogs kept on one hand, and between the county of residence and ownership of fox skin products on the other hand. The p value of the factor "county of residence" increased from 0.051 in single factor analysis to 0.009 in multiple factors regression. When the "county of residence" factor was excluded, the number of dogs kept was found significant (p=0.022, OR=1.722) by forward stepwise multiple regression and ownership of fox skin products was found significant (p=0.017,OR=6.583) by backward stepwise multiple regression. These two factors might be the key differences between farmers from Shiqu County and Ganzi County, and the "county" risk factor could sum the significance of the two factors and become more significant in multiple regression analysis. This is the first time in China that epidemiological analysis does suggest that the fox might play a significant role in AE transmission to humans. Geographical factors might however combine with behavioral factors to lead to such a difference between counties, since it might be assumed that ownership of fox products might be a consequence of higher number of foxes in the area, related to environmental causes.

In Tibetan rural areas, in addition to contamination through the local *E.multilocularis* cycle, contamination through dogs imported from other herdsmen communities cannot be ruled out. When we did household visits, we found that the transfer of dogs between communities, even between provinces, were not rare. For example, two herdsmen settlements in Yiniu Township, Shiqu County, reported that most of their dogs died in 2002. Almost all the dogs they kept in 2003 came from other settlements. A businessman in Arizha Township, Shiqu County, mentioned that his dogs were regularly sold to Heilongjiang Province, because people there loved to keep Tibetan big dogs. Heilongjiang is known to have AE infection reported in humans; however no final or intermediate host infection was ever reported (Li and Shi, 1985; Yu et al, 1994; Wen et al., 2002; Vuitton et al., 2003).Transfer of infected dogs might contribute to farmers' infection. Active transmission has been recorded in farmers of Han communities in South Gansu (Craig et al. 1992; Craig, 2000). This has been interpreted as the result of deforestation leading to the extension of favorable habitat to cyclic small mammal intermediate hosts (Giraudoux et al., 2002, 2003). However, the process by which such newly favorable environment is contaminated with *E. multilocularis* remains unclear. Dog trade may be an important way for the parasite to be spread in areas where it was not present before. In the United States, a shipment of foxes and coyotes was confiscated in South Carolina by federal and state wildlife authorities in 1989; *Echinococcus multilocularis* was identified in 3 of 44 red foxes that had been translocated illegally from eastern Indiana and western Ohio and were to be released into fox hunting enclosures in southeastern states. Subsequent investigation revealed that the practice of translocation of foxes from areas where E multilocularis is curretnly enzootic into souteastern states is apparently common. There is no evidence that the tapewom has become established yet in soueastern states; however, if the practice of translocation cointinues it almost certainly will be (Schantz, 1993).

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Table 1 Age- and gender-specific infection rates of the surveyed population

	Infection rates						Chi-square	P
	Age≤10	10＜age≤20	20＜age≤30	30＜age≤40	40＜age≤50	Age＞50		
All surveyed population	0.5% (4/740)	0.8% (11/1422)	1.9% (30/1573)	3.5% (53/1522)	4.4% (42/952)	8.8% (83/940)	157.2	<0.001
Male	0.5% (2/366)	0.6% (4/692)	1.3% (10/744)	2.8% (20/721)	3.4% (15/443)	8.7% (40/459)	88.9	<0.001
Female	0.5% (2/371)	1.0% (7/729)	2.4% (20/826)	4.1% (33/799)	5.3% (27/508)	9.0% (43/480)	73.5	<0.001
All Herdsmen	1.3% (4/310)	1.1% (5/445)	2.8% (19/676)	6.3% (39/621)	7.0% (28/401)	11.6% (59/509)	78.7	<0.001
Male	1.4% (2/148)	1.0% (2/210)	1.7% (5/300)	5.6% (16/286)	4.8% (8/168)	12.5% (32/256)	51.2	<0.001
Female	1.3% (2/159)	1.3% (3/235)	3.7% (14/375)	6.9% (23/334)	8.6% (20/232)	10.7% (27/252)	33.9	<0.001
All Farmers	0% (0/22)	1.5% (1/65)	0% (0/138)	1.3% (2/154)	1.3% (2/153)	5.4% (7/129)	12.9	0.025
Male	0% (0/11)	0% (0/30)	0% (0/57)	0% (0/65)	0% (0/52)	5.7% (3/53)	12.3	0.031
Female	0% (0/11)	2.9% (1/35)	0% (0/81)	2.2 % (2/89)	2.0 % (2/101)	5.3% (4/76)	5.3	0.386
Town population	0% (0/141)	1.3% (2/150)	1.4% (10/690)	1.7% (12/707)	2.1% (8/381)	2.3% (17/293)	25.3	<0.001
Male	0% (0/71)	0% (0/109)	1.1% (4/353)	1.2% (4/343)	1.4% (3/211)	3.4% (5/148)	7.5	0.184
Female	0% (0/70)	4.9% (2/41)	1.8% (6/336)	2.2% (8/363)	2.9% (5/170)	8.3% (12/145)	19.4	0.002
Student	0% (0/258)	0.4 (3/761)	0% (0/24)	—	—	—	1.117	0. 572
Male	0% (0/132)	0.6% (2/341)	0% (0/10)	—	—	—	0.836	0.658
Female	0% (0/126)	0.2% (1/420)	0% (0/14)	—	—	—	0.334	0.846

Table 2 Gender-stratified analyses including age and living place using stepwise multiple logistic regressions (2,850 male cases, 3,086 female cases included)

Male population	Parameter estimate	Standard Error	Wald	Degree of freedom	P	Odds ratio
Age	0.049	0.007	52.503	1	<0.001	1.050
Farmers vs. herdsmen	-1.586	0.597	7.057	1	0.008	0.205
Urban vs. herdsmen	-1.281	0.285	20.182	1	<0.001	0.278
Farmers vs. Urban	-0.305	0.635	0.230	1	0.632	0.737
Intercept	-4.949	0.341	211.155	1	<0.001	0.007
Female population	**Parameter estimate**	**Standard Error**	**Wald**	**Degree of freedom**	**P**	**Odds ratio**
Age	0.038	0.005	50.811	1	<0.001	1.039
Farmers vs. herdsmen	-1.114	0.357	9.766	1	0.002	0.328
Urban vs. herdsmen	-0.701	0.209	11.209	1	0.001	0.496
Farmers vs. Urban	-0.413	0.383	1.165	1	0.280	0.662
Intercept	-4.268	0.256	276.953	1	<0.001	0.014

Table 3 Single and multiple factor analysis using stepwise logistic regression for herdsmen communities

Risk factors		AE prevalence	Single factor analysis results		Multiple factors analysis results	
			P	Odds ratio	P	Odds ratio
County	Ganzi County	3.2% (14/440)	Reference	—	—	—
	Shiqu County	5.6% (140/2522)	0.042	1.788	—	—
Gender	Male	4.8% (65/1368)	Reference	—	—	—
	Female	5.6% (89/1587)	0.297	1.191	—	—
Age		—	<0.001	1.041	<0.001	1.036
Education	No education	6.2% (139/2239)	Reference	—	—	—
	Primary school education	3.2% (13/403)	0.020	0.504	—	—
	Middle school education	0.7% (2/279)	0.002	0.109	—	—
	College education and above	0% (0/24)	0.549	0.011	—	—
No. of dogs kept		—	0.060	1.133	—	—
Dog kept by neighbors	Yes	5.6% (147/2630)	Reference	—	—	—
	No	3.6% (6/165)	0.289	0.637	—	—
Fox skin products	No	4.4% (28/639)	Reference	—	—	—
	Bought or donated	5.8% (124/3132)	0.164	1.348	—	—
	Self hunting	0% (0/29)	0.545	0.016	—	—
Water sources	Stream	6.9% (88/1271)	Reference	—	—	—
	River	5.0% (40/794)	0.085	0.713	—	—
	Well	2.4% (11/458)	0.001	0.331	—	—
	Pond	0 (0/14)	0.545	0.027	—	—
	Tap water	4.4% (12/271)	0.133	0.623	—	—
Nomadic life style	Not nomadic	5.4% (85/1564)	Reference	—	—	—
	Nomadic with tent	4.6% (17/371)	0.509	0.836	—	—
	Nomadic living in winter house	5.9% (51/869)	0.655	1.085	—	—
Income	Income<2,000 Yuan	6.3% (83/1313)	Reference	—	—	—
	2000≤Income<5,000	5.8% (61/1051)	0.601	0.913	—	—
	5,000≤Income<10000	3.2% (8/249)	0.060	0.492	—	—
	Above 10,000	0.5% (1/186)	0.012	0.083	—	—
Livestock raising	No	3.7% (20/545)	Reference	—	—	—
	Yes	5.9 (130/2214)	0.044	1.637	—	—
Hand washing before eating	No	6.4% (129/2007)	Reference	—	—	—
	Always	3.2% (14/435)	0.011	0.484	—	—
	Sometimes	2.2% (8/358)	0.003	0.333	—	—
Drinking non-boiled water	No	6.7% (66/983)	Reference	—	—	—
	Sometimes	4.8% (47/498)	0.071	0.701	—	—
	Always	4.5% (38/842)	0.044	0.657	—	—
Preventing fly from food	Yes	0.7% (4/557)	Reference	—	Reference	—
	No	6.6% (147/2242)	<0.001	9.685	<0.001	8.598
Playing with dogs	Always	5.6% (45/804)	0.008	2.977	—	—
	Sometimes	6.1% (99/1632)	0.003	3.262	—	—
	Never	1.9% (7/359)	Reference	—	—	—

1) "—" : Not applicable; 2) the results were the same using forward or backward conditional methods, and with or without "county of residence" factor

Table 4 Single and multiple factor analysis using stepwise logistic regression for farming communities

Risk factors		AE prevalence	Single factor analysis results		Factors found significant by multiple factors regression	
			P	Odds ratio	P	Odds ratio
County	Ganzi County	1.3% (7/537)	Reference	—	Reference	—
	Shiqu County	4.0% (5/124)	0.051	3.181	0.009 a	5.167
Gender	Male	1.1% (3/268)	Reference	—	—	—
	Female	2.3% (9/393)	0.279	2.070	—	—
Age		—	0.001	1.076	0.001 abc	1.078
Education	No education	1.7% (8/466)	Reference	—	—	—
	Primary school education	1.9% (2/107)	0.914	1.090	—	—
	Middle school education	2.3% (2/87)	0.709	1.347	—	—
	College education and above	—	—	—	—	—
No. of dogs kept		—	0.024	1.636	0.022b	1.722
Dog kept by neighbors	Yes	2.0% (12/600)	Reference	—	—	—
	No	0% (0/36)	0.818	0.002	—	—
Fox skin products	No	0.6% (2/347)	Reference	—	—	—
	Bought or donated	3.6% (10/280)	0.017	6.389	0.017c	6.583
	Self hunting	0% (0/8)	0.886	0.047	—	—
Water sources	Stream	3.1% (2/65)	Reference	—	—	—
	River	1.3% (4/318)	0.298	0.401	—	—
	Well	4.1% (2/49)	0.774	1.340	—	—
	Pond	0% (0/16)	0.817	0.003	—	—
	Tap water	2.1% (4/190)	0.657	0.677	—	—
Income	Income<2,000 Yuan	2.9% (7/239)	Reference	—	—	—
	2000≤Income<5,000	1.2% (3/301)	0.115	—	—	—
	5,000≤Income<10000	1.0% (1/82)	0.407	—	—	—
	Above 10,000	6.7% (1/15)	0.435	—	—	—
Livestock raising	No	3.5% (6/171)	Reference	—	—	—
	Yes	1.3% (6/464)	0.081	0.360	—	—
Hand washing before eating	No	2.1% (8/373)	Reference	—	—	—
	Always	1.1% (1/90)	0.531	0.513	—	—
	Sometimes	1.7% (3/175)	0.738	0.796	—	—
Drinking non-boiled water	No	4.5% (5/112)	Reference	—	—	—
	Sometimes	1.7% (3/176)	0.181	0.371	—	—
	Always	1.1% (4/349)	0.040	0.248	—	—
Preventing fly from food	Yes	1.5% (5/328)	Reference	—	—	—
	No	2.3% (7/310)	0.498	1.492	—	—
Playing with dogs	Always	3.8% (2/52)	0.124	3.869	—	—
	Sometimes	3.1% (6/193)	0.082	3.104	—	—
	Never	1.0% (4/391)	Reference	0.258	—	—

1) "—" : Not applicable; 2) "a": results of forward and backward multiple regression that included "county of residence" factor; "b": results of forward multiple regression that did not include "county of residence" factor; "c": results of backward multiple regression that did not include "county of residence" factor.

Table 5 Single and multiple factor analysis using stepwise logistic regression for urban population

Risk factors		AE prevalence	Single factor analysis results		Factors found to be significant in multiple factors analysis	
			P	Odds ratio	P	Odds ratio
County	Ganzi County	1.0% (13/1307)	Reference	—	—	—
	Shiqu County	3.4% (36/1055)	<0.001	3.516	—	—
Gender	Male	1.3% (16/1235)	Reference	—	Reference	—
	Female	2.9% (33/1125)	0.007	2.302	0.009	2.345
Age		—	<0.001	1.046	0.001	1.031
Ethnic group	Tibetan	2.7 (46/1720)	0.003	5.853	—	—
	Han	0.5% (3/642)	Reference	—	—	—
Education	No education	4.8% (28/589)	Reference	—	—	—
	Primary school education	1.7% (5/293)	0.031	0.348	—	—
	Middle school education	1.1% (15/1314)	<0.001	0.231	—	—
	College education and above	0.6% (1/156)	0.045	0.130	—	—
No. of dogs kept		—	<0.001	1.429	—	—
Dog kept by neighbors	Yes	2.2% (46/2078)	0.309	1.841	—	—
	No	1.2 (3/274)	Reference	—	—	—
Fox skin products	No	1.3% (12/935)	Reference	—	—	—
	Bought or donated	2.7 (37/1377)	0.025	2.124	—	—
	Self hunting	0% (0/10)	0.805	0.057	—	—
Water sources	Stream	5.7% (18/314)	Reference	—	Reference	—
	River	3.5% (12/339)	0.185	0.603	.166	.550
	Well	1.7% (6/355)	0.008	0.283	.033	.354
	Pond	4.8% (1/21)	0.853	0.822	.677	1.581
	Tap water	0.9% (12/1304)	<0.001	0.153	.001	.267
Income	Income<2,000 Yuan	3.4% (20/591)	Reference	—	—	—
	2000≤Income<5,000	2.2% (19/883)	0.152	0.628	—	—
	5,000≤Income<10000	1.1% (8/702)	0.008	0.329	—	—
	Above 10,000	1.4% (2/148)	0.209	0.391	—	—
Livestock raising	No	1.2 (20/1601)	Reference	—	—	—
	Yes	3.7% (26/705)	<0.001	3.027	—	—
Hand washing before eating	No	4.0% (28/702)	Reference	—	—	—
	Always	1.0% (10/1040)	<0.001	0.234	—	—
	Sometimes	1.9 (11/587)	0.031	0.460	—	—
Drinking non-boiled water	No	2.0% (23/1147)	Reference	—	—	—
	Sometimes	2.5% (21/843)	0.467	1.248	—	—
	Always	1.5% (5/337)	0.538	0.736	—	—
Preventing fly from food	Yes	1.2% (18/1463)	Reference	—	—	—
	No	3.6% (31/865)	<0.001	2.984	—	—
Playing with dogs	Always	4.8% (12/148)	<0.001	6.943	.004	4.550
	Sometimes	3.0% (29/967)	<0.001	4.222	.024	2.826
	Never	0.7% (8/1102)	Reference	—	Reference	—

1) "—" : Not applicable; 2) the results were the same using forward or backward conditional methods, and with or without "county of residence" factor.

Table 6 Number of dogs kept and ownership of fox skin products in Ganzi and Shiqu farmers' communities

Dog ownership	Ganzi			Shiqu			F	P
	Mean	N	Standard Deviation	Mean	N	Standard Deviation		
Number of dogs per households	0.97	537	0.79	1.34	124	1.42	15.3	<0.001

Possession of fox skin	Ganzi			Shiqu			Chi-square	P
	No fox skin	Bought or donated	Self hunting	No fox skin	Bought or donated	Self hunting		
Proportion of households	61.6% (331/537)	37.1% (199/537)	1.3% (7/537)	16.3% (16/98)	82.7% (81/98)	1.0% (1/98)	70.3	<0.001

Chapter 2 History and current management of grazing practices

Guiding questions: 1) What is overgrazing? 2) How can we measure it? 3) What is the situation of grazing practice currently and historically in the Tibetan pastures?

2.1 Definition of overgrazing and origin of overgrazing

In ecology, overgrazing is defined as "*a type and degree of utilization of a pasture which prevents the complete regeneration of the palatable plants*" (e.g. because they have no chance to accumulate and store nutrients for re-growth) (Holzner and Kriechbau, 2000). Overgrazing is defined as occurring where there is concomitant vegetation change and loss of animal productivity arising from the grazing of land by herbivores (Wilson and Macleod, 1991).

Overgrazing is the mode of utilization, a change of vegetation is its indicator, reduction of the productivity is its short-term effect, and “desertification” is the long-term effect (Holzner and Kriechbau, 2000). The term “overgrazing” describes only (and both) the direct impact on the pasture and the reasons for its degradation. The causes of overgrazing are complex and varied; they are not ecological, *sensu stricto*, but rather cultural, social and economic in nature. Some of the usually cited causes were: 1) increase in human population and animal density, 2) loss of control or abandonment of the equilibrium between herd size and pasture size, and 3) change or abandonment of the seasonal grazing pattern (Holzner and Kriechbau, 2001).

The definition of overgrazing given by Holzner and Kriechbau (2000) incorporates some major facts that are still under heavy discussion and have not reached conclusions so far. "*Vegetation change is its indicator*", as stated by Holzner and Kriechbau (2000) is too conclusive while some other authors pointed out that "*some degree of vegetation change was almost universal*" and "*evidence of vegetation change per se was insufficient evidence for overgrazing*" (Wilson and Macleod, 1991). Furthermore, some others argued that, conversely vegetation change was actually due to the invasion of small mammals and/or climate changes (Chen et al, 1998; Cheng et al, 1998; Wang G, et al., 2001; Li, 1995; Hou, 2001). Small mammal herbivores may consume as much as 60% (Migula et al., 1970) to 80% (Taylor and Loftfield, 1942) of the total annual primary plant production. It comes to desertification, which was used as a key feature of long term overgrazing by Holzner and Kriechbau (2000), was thus partially attributed to global climate change and invasion of small mammals (Chen et al, 1998; Cheng et al, 1998; Wang G, et al., 2001; Miller, 1999; Li, 1995; Hou, 2001).

In addition to the difficulties mentioned above in reaching a consensus on its definition, quantification of overgrazing is also an uneasy task (Wilson and Macleod, 1991). Under the assumptions of vegetation change and desertification as indicators of overgrazing, but nevertheless with few efforts to link these indicators to overgrazing, Holzner and Kriechbau (2000) used them to categorize pastures into "*optimal pastures*", "*recent overgrazing*", "*degraded pastures*" (centuries of overgrazing) and "*desertified areas*". "Recent overgrazing" was further divided into 5 levels of RDP (recently degraded pastures) based on vegetation change and desertification of pastures. Some examples taken from the paper clearly show that no real quantification was proposed: 1) RDP1: somewhat overgrazed, but desertification still far away. Regeneration seems to be possible after improved utilization; estimated recovery phase within about 10 years. 2) RDP3: overgrazed, desertification can be expected within one human generation. Regeneration seems to be possible, necessary time span difficult to judge, but probably within one generation. 3) RDP5: severely overgrazed, degree of vegetation destruction close to desertification. Regeneration theoretically possible, but only within a long time span (Holzner and Kriechbau, 2000). It seems that Holzner and Kriechbau (2000, 2001) used "overgrazing" to define "overgrazing"; furthermore, they did not try to sort out a key conception of "current overgrazing "; and if there is no way to figure out "current overgrazing", we may wonder if it is convincing that past overgrazing can be identified… and we are tempted to say: "hardly".

Wilson and Macleod (1991) put forward a way of quantifying overgrazing. They proposed an experiment over a range of stocking rates, ideally conducted on a continuous basis for 5 to 10 years to encompass a range of rainfall sequences and give sufficient time for treatment effects to become manifest. Such an experiment would ideally be conducted with young animals that are more responsive to differences in nutrition. The evidence of deleterious change in the vegetation, or overgrazing, would appear as a loss of linearity in the average production-stocking rate relationship; it might subsequently be confirmed by a further period when all paddocks are stocked at the economic optimum stocking rate. Alternatively, when the focus is for rangeland pastures that are hypothesized to have changed prior to commencement of experiment, the evidence sought for would consist in a reduced optimum stocking rate. This approach is an attempt to verify "overgrazing at present and in the past" from the point view of livestock industry. But, it seems that the method tended to view "average production-stocking rate" as optimal stocking rate which might be not proper for communities where average production-stocking rate had already led to overgrazing; the method is also very very time-consuming because it would take a long period of time; in addition, it has just been theoretically explored and has not been justified by further researches.

Some others used livestock husbandry indicators, e.g. "*units of livestock/hectare*" to quantify *grazing or overgrazing pressure* on pastures (Ho, 1998): the higher ratio of the figure, the severer overgrazing of the pasture. Assuming that herdsmen want to maximize their personal and immediate benefit from the common pastures, they would raise as many livestock units on the pastures as possible; then assuming all pastures with the same original productivity, the higher figure of "sheep units/ha" in a pasture would actually be an indication of higher productivity of the pasture after a period of grazing by livestock. But in reality, it is hard to know the original productivity of pastures; hence the reliability of the use of this husbandry indicator is doubtful. With this method Ho (1998) compared livestock density in Ningxia with that of North China, which is not convincing at all, because of the different productivity capacities among pastures in different regions. Another example shows that the husbandry indicator could be totally misleading when property rights arrangement is not considered: in 1970s when all livestock and pastures belonged to communes in Shiqu County (Editorial Commission of Shiqu County Record, 1997), the majority of herdsmen tended to stay in winter pastures or low altitude pastures and did not go to summer pastures at all in the year…This led to great shortage of forage in winter pastures and conversely to oversupply in summer pastures. Winter pastures were thus described as overgrazed. However, in these years the number of livestock was not considered when the number of livestock was too high but it was managed differently or the pastures were overgrazed. Li (1995) stated that the productivity of pastures decreased dramatically and the number of livestock kept decreasing from 1,050 thousands in 1980 to 770 thousands in 1993, because of the invasion of small mammals to pastures and overgrazing. If these figures were correct, can we say that the pastures in 1980 when there was a bigger livestock population were more overgrazed than the pastures in 1993 when there was a smaller population? Hardly. Thus, when these ecological and husbandry indicators are applied, socio-economical situation should be seriously considered, given the socio-economics origin of overgrazing.

Another definition of overgrazing is given as "*to permit animals to graze (vegetation cover) excessively, to the detriment of the vegetation*" (The American Heritage Dictionary of the English Language, Fourth Edition 2000), in which "*to permit*" is a stress on human behavior, and thus on the socio-economics aspect of overgrazing. Overgrazing is used as the canonical example of the so-called "*Tragedy of the commons"*. The tragedy of the commons is a metaphor that illustrates the sub-optimal use or even destruction of public resources (the "commons") by private interests when the best strategy for individuals conflicts with the common good (The American Heritage Dictionary of the English Language, Fourth Edition 2000).

According to Hardin (1968), the tragedy of the commons develops in this way. Picture a pasture open to all. It is to be expected that each herdsman will try to keep as many cattle as possible on the commons. Such an arrangement may work reasonably and satisfactorily for centuries because tribal wars, poaching, and disease keep the numbers of both man and beast well below the carrying capacity of the land. Finally, however, comes the day of reckoning, that is, the day when the long-desired goal of social stability becomes a reality. At this point, the inherent logic of the commons remorselessly generates tragedy. As a rational being, each herdsman seeks to maximize his gain. Explicitly or implicitly, more or less consciously, he asks, “What is the utility to me of adding one more animal to my herd?” This utility has one negative and one positive component. 1) The positive component is a function of the increment of one animal. Since the herdsman receives all the proceeds from the sale of the additional animal, the positive utility is nearly +1. 2) The negative component is a function of the additional overgrazing created by one more animal. Since, however, the effects of overgrazing are shared by all the herdsmen, the negative utility for any particular decision-making herdsman is only a fraction of –1. Adding together the component partial utilities, the rational herdsman concludes that the only sensible course for him to pursue is to add another animal to his herd. And another, and another… But this is the conclusion reached by each and every rational herdsman sharing a commons. Therein is the tragedy. Each man is locked into a system that compels him to increase his herd without limit-in a world that is limited in its resources. Freedom in a commons brings ruin to all (Hardin, 1968). Besides Hardin, a number of scholars also thought that a resource held under a common property resource (CPR) regime was inherently inefficient since individuals did not get proper incentives to act in a socially efficient way (Gordon, 1954; Scott, 1955).

Economically, the primary source of conflict is scarcity. Just as Hardin mentioned, when the long-desired goal of social stability becomes a reality, which brings about big growth in both human and livestock population, the grassland thus becomes a scarce resource. Then come the conflict and overgrazing on the common pastures. In this situation, just as Hayek (1973) explains, "the understanding that "*good fences make good neighbors*", that is, that man can use their own knowledge in the pursuit of their own ends without colliding with each other only if clear boundaries can be drawn between their respective domains of free action …". Therefore, according to Hardin and basic economics assumption (scarce resources), we can put forward two basic constraints when overgrazing happens: 1) pastures are scarce resources in communities where livestock raising is a key industry; and 2) there is a common ownership of pastures for grazing. These two major features will be our working concept of overgrazing for our research.

Some argued that the problem of overexploitation and degradation of common property resources could be resolved only by creating and enforcing private rights (Demsetz, 1967; Cheung, 1970; Johnson, 1972; Smith, 1981; Ho, 1999). Here comes a question, what is the definition of private property rights? According to Cheung (2000), it includes income rights, exclusive use rights, and exclusive rights to transfer his property to any people he thinks proper. Accordingly, commons means that nobody in the commons can exclude anybody to access to its use; every one can use it for free. It is very difficult, or even impossible, for people to transfer the commons or part of the commons to others, which means for people in the commons that there is almost no way for them to quit the system economically.

Some argued that the common grazing lands in Hardin's classic 'tragedy of commons' were well looked after for many centuries, before they declined for reasons unrelated to any inherent flaw in the commons system (Cox, 1985). It was said that the failure of commons institution was because of internal reasons, such as the inability of the users to manage themselves, or because of external reasons, for example incursion of outsiders (Dove, 1993). However, in his paper, Cox did not mention if the pastures were scarce resource or not when commons worked well. For the latter, one can easily argue that the best solution is to push users managing themselves by privatization of pastures; also, the incursion of outsiders is a very weak cause to be used to explain universal commons problem. For the issue of Tibetan pastures management, some also argued that traditional way of pasture management had been sustained for hundred and thousand years (Miller, 1999) in spite of increasing population pressure that had made the pastures scarce resources.

2.2 Property rights and grazing practices: history and current aspects

It was suggested that, at least from year 600 AC to early 1950s, the Tibetan pastures were generally owned by tribes (Chen et al. 2002). Livestock were private properties from year 100 AC. There was a philosophical fable named “story about monkeys and birds” that convinced people to adopt commons property rights. The story is the following. There was a holy mountain named Gengzang. Lions occupied the top of the mountain, in mountain banks lived birds, and beasts stayed at the foot of the mountain. One day, the monkeys living in the forest at the foot of the mountain went to mountain bank to search food, the birds made stern warning. Then the monkeys argued that Gengzang was a mountain for the sake of all lives, it was not necessary that it belonged to anybody. Although the lions lived on the top of mountain, it was a natural settlement, not bought by them; on the mountain bank there lived the birds, it was a natural gathering and not because of donation by anybody; in the foot of mountain, there lived the beast naturally but not because of any purchase with gold and silver; the monkeys were born there, it was because of predefined fate, and not because of being invited. Therefore, no matter where it was in this mountain, the forest, the grass, the wood, the flower and fruits, all shared all of them; and it was not necessary to say which were yours and which were ours. Until early 1950s when collectivization did not begin, Tibetan herdsmen in Ruo'ergai County in Sichuan Province still said that pastures belonged to tribes, not to the local officials of previous government (Republic of China). When distributing pasture use rights and resolving dispute on use rights of pastures, the head of tribe needed to summon some people concerned to discuss, which indicates that at that time the head did not think the pastures belonged to himself. There were four ways to distribute the pastures use rights before 1950s. 1) *Free grazing rights, for community with big pastures*: herdsmen could have their livestock to graze anywhere they want. Who came first to a pasture used it but not exclusively. 2) *Seasonal redistribution of pastures among* *herders*. When it came to a date to move to summer or winter pastures, the highest-level head of the community called lower level heads to discuss the route and place for each small tribe to graze, then the lower level heads did the same thing for herdsmen. 3) *Permanent distribution through issuing licenses for pastures use rights* so that each households had comparative fixed pastures. In 1958, according to records, herdsmen in Ashiqiang Tribes in Guoluo prefecture, Qinghai province, had used pastures licensed to each household for 8-9 generations. 4) *Seasonal distribution combined with permanent distribution*. For example in Ruo'ergai County, Sichuan Province, herdsmen had permanent pastures belonging to each household in winter pastures, but summer pastures were distributed annually based on small tribe groups. Generally, the permanent pastures were never private properties, because if the tribe could find any proper reason, for example, when the number of livestock of a family decreased, part of the pastures used by the family could be distributed to other families with more livestock. However, in 1958, very small parts of winter pastures were private properties to some extent because they were exclusive and could be sold in North Tibet and South Qinghai, although the selling was under tight control of tribes (Chen et al.2002).

Husbandry was collectivized in the period between middle 1950s and just after the end of the Cultural Revolution (1966-1976), which means that livestock and pastures all belonged to commune. After 1978, the livestock was privatized but the pastures were still commune properties. In 1983, households contracted for pastures and “group tenure of pastures" was attempted and the course got steam in middle 1990s (Shiqu County Editorial Commission for county record, 2000; Rangtang County Editorial Commission for country record, 1997; Ruo’ergai County Editorial Commission for country record, 1996; Hongyuan County Editorial Commission for county record, 1996). In a recent cross-sectional investigation, group tenure arrangements and ‘fuzzy’ boundaries were identified as key features of current property rights for Chinese pastures (Banks, 2001). However, according to Chinese Law for Pastures Management (2003), the household-contracted pastures can never be viewed as real private property, because the tenure is limited to 50 years (Chinese law for contracted land, 2003) and any transfer of the pasture use rights can not exceed the tenure and should get permission from local collective authorities. It seems that some deem household-contract system as privatization (Foggin and Smith, 1996; Miller, 1999), which may be far from the reality in Western Chinese Pastures. Especially when the pastures are actually commons, it is very hard to imagine that people can transfer the pasture use rights, which is a key feature of private property. It was suggested that current pasture property rights arrangement was suitable because of its benefits including facilitation of economies of size with respect to herding labor, equitable household access to resources and insurance against economic risk (Banks, 2001). However, our observation indicates that in vast Tibetan pastoralist regions, it is costly to define the boundaries and to defend the boundaries if one wants to distribute the pastures on an individual household level rather than group level. Cheung indicated that "*commons property rights saved the cost of defining private property rights and enforcing the rights" …… "this cost perhaps being a luxury that some communities could not afford"* (Cheung, 2000).

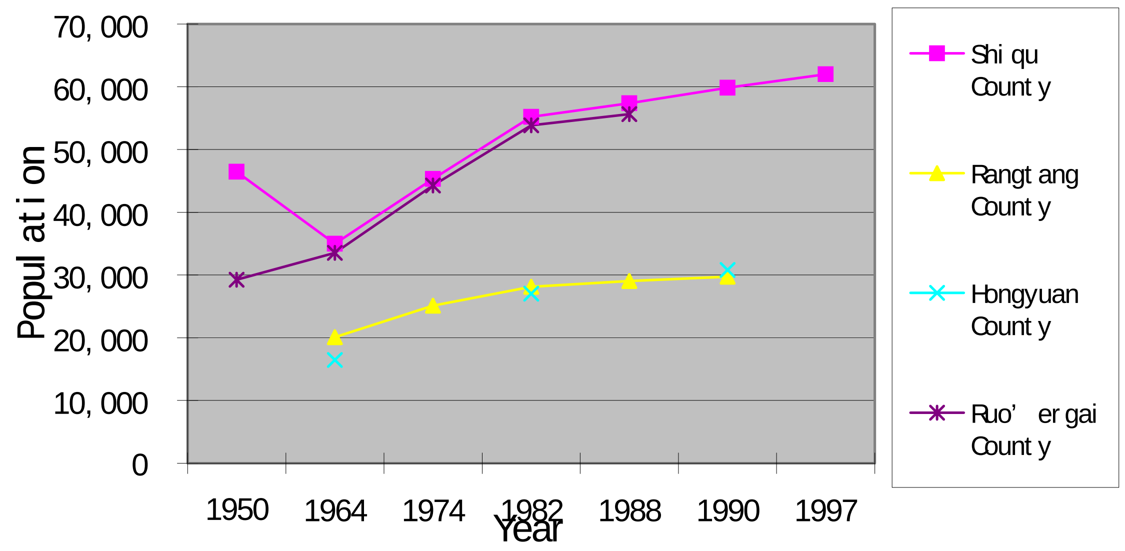
2.3 Socio-economical correlates of overgrazing

Based on above paragraphs, mainly from the description of "the tragedy of commons" (Hardin, 1968), we could figure out two very basic indicators of overgrazing: 1) scarcity of pastures, and 2) common ownership of the pastures. Those two indicators are both "a must" for overgrazing occurring. To further extend those two indicators, one can put forward other indicators including conflicts and fighting for the competitively using of pastures, which not only indicate the consequences of scarcity of pastures but also of the vaguely defined ownership of pastures. Other indicators also imply a declining availability of pastures for grazing, such as increasing number of livestock and increasing human population.

The fighting happened mostly among tribes rather than among individuals for occupying pastures before 1950s (Chen et al., 2002). However, it became a big problem when, after collectivization of all livestock and pastures in late 1950s, the pastures were commons while the number of livestock was huge and was privatized in the late 1970s and early 1980s. For example in Shiqu County, it is recorded that when "*the livestock is private property, the pastures are commons*", every family tried to raise as much livestock as possible and competed with each other to graze good pastures. Conflicts happened very often and some even turned into armed fighting among Tibetan herdsmen (Shiqu County Editorial Commission for County Record, 2000). In Hongyuan County, it was a growing problem since 1960s among neighboring counties, townships and villages. When it came to 1980s, the problem became more severe (Hongyuan County Editorial Commission for County Record, 1996). But, it also depended on the specific situation, for example, in Rangtang County, few conflicts were recorded for use right of Tibetan pastures among herdsmen (Rangtang County Editorial Commission for country record, 1997).

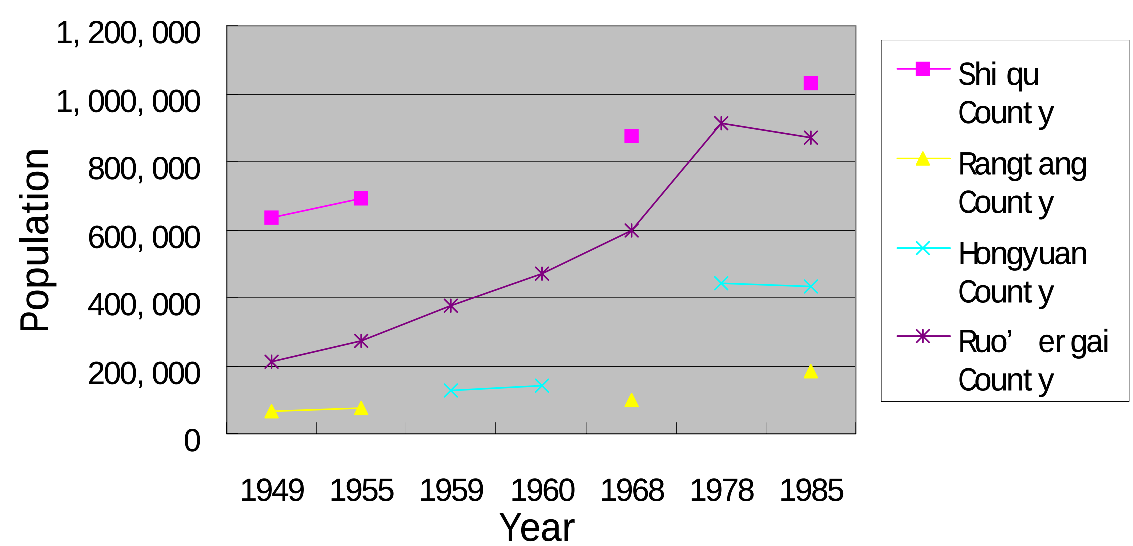
During the same period, from 1949 to late 1980s, there was a steady growth of human population and livestock population, which means that the pastures in Tibetan plateau area became less accessible without cost (See Figure II-1, Figure II-2). In Shiqu County, it was recorded that because the number of livestock exceeded the carrying capacity of the pastures, when natural disasters occurred, for example, drought or heavy snow that reduced grass growth dramatically, the livestock had much less grass to graze and suffered great loss in 1986 and 1996 (Shiqu County Editorial Commission for county record, 2000). In the middle of the 1980s, in response to increasing conflicts over pastures use rights and the deterioration of pastures and to promote good neighborhood, a new law (Chinese Pasture Law) was issued to ask for defining the boundary among counties, among townships, and among villages. The new law also stated that one household or a group of households (group tenure) were being responsible for contracting with government for use rights of pastures.

Figure II-1 Human population changes in four Tibetan counties



Data are quoted from: Shiqu County Editorial Commission for county record, 2000; Rangtang County Editorial Commission for country record, 1997; Ruo'ergai County Editorial Commission for country record, 1996; Hongyuan County Editorial Commission for county record, 1996.

Figure II-2 Livestock population changes in four Tibetan counties



Data are quoted from: Shiqu County Editorial Commission for county record, 2000; Rangtang County Editorial Commission for country record, 1997; Ruo'ergai County Editorial Commission for country record, 1996; Hongyuan County Editorial Commission for county record, 1996.

In summary: 1) No reliable and well assessed ecological methods are applicable for identifying the existence of overgrazing or accurately measuring overgrazing; 2) Socio-economical concept of overgrazing provides two dimensions for identifying overgrazing: scarcity of pastures in communities where livestock raising is the key industry and common usage of pastures; 3) Tibetan pastures have been scarce resources and commons for a long time; 4) according to the socio-economical concept of overgrazing, it may be assumed that overgrazing does exist now and has long existed in the Tibetan pastoralist communities.

Chapter 3 Grazing practice as a potential risk factor for *E.multilocularis* transmission

Guiding questions: 1) What is the relationship between grazing practice and population of small mammals around the world and in China? 2) How does overgrazing influence the population density of small mammals in the surveyed Tibetan communities? 3) How does the population density of small mammals affect E. multilocularis infection in dogs in the Tibetan communities? 4) How is overgrazing linked to AE prevalence in human in the Tibetan communities?

3.1 Interaction between grazing practice and small mammal populations around the world

The interaction between grazing practice and small mammal populations were studied widely throughout the world. The focuses of these researches were on the impact of grazing on abundance and diversity of species of small mammals. The results were different and sometimes even contradictory.

In several studies, globally, a decrease in either the total population or of the species diversity of small mammals was observed in grazed and/or overgrazed areas.

In the United States in the period of 1976 and 1977, on the same so-called "Idaho

National Engineering Laboratory site" (INEL site), researches were done to understand the grazing effects on the abundance of small mammals. Some found that grazing led to lower abundance and species of small mammals (Reynolds and Trost 1980). However, other two studies in the same place and in the same period that also addressed the effects of livestock grazing on populations of wildlife on the INEL site found that there was no evidence that differences among the areas actually resulted from the land use practices (i.e. grazing) (Johnson, 1982). The studies were performed by measuring indices of small mammal abundance among areas where different practices had occurred prior to initiation of study (Johnson, 1982). It was argued that the impact of grazing on diversity or abundance of small mammals highly depended on the composition of the initial small mammal community, but generally grazing led to less biomass of small mammals, which as was revealed in Washington State, Montana, Colorado and Oklahoma, USA (Grant 1982). It was showed that in the tall grass grassland of the plains, reduction in grass cover resulted in a decrease in total small mammal biomass, and an increase in species diversity, and a shift from litter-dwelling species with relatively high reproductive rates to surface-dwelling species with relatively low reproductive rates; a change similar to that observed along a gradient from high to low cover across grassland types. *In mountain grasslands*, however, reduction in cover resulted in a decrease in both total small mammal biomass and species diversity and, while species composition shifted from litter-dwelling to surface-dwelling species, there was a relative increase in the biomass of species with higher reproductive rates. *In shortgrass and buchgrass grasslands*, mall mammal communities did not exhibit the pronounced changes in response to cover reduction that were observed in tall grass or mountain grasslands, or along a cover gradient between grass types (Grant 1982).

In the Great Salt Desert, *North America*, by conducting a series of studies at heavily and lightly grazed sites to investigate effects of cattle grazing on desert rodent relative abundances, home range sizes and microhabitat in the shrub communities, it was found that different levels of grazing were associated with differences in relative abundance of some species of rodents through monitoring of rodent populations with repeated live trapping. Especially, *Dipodomys merriami* was significantly more abundant in lightly grazed areas. It was showed that cattle, by preferentially feeding on certain plants, could create conditions that were more suitable for some species of rodents, while reducing important microhabitat for other species (Jones and Longland, 1999).

In South Africa, vegetation changes superimposed by grazing and their effect on small mammals were studied on grazed farmland and an adjacent, 10-year livestock enclosure. Plains and drainage line habitats were compared by monitoring vegetation height and cover, and small mammal species composition and abundance along transects. Animals were captured by live trapping. Vegetation cover was low on the grazed compared to the ungrazed study site, but vegetation height did not differ. Five species of small mammals were captured, namely *Gerbillurus paeba, Macroscelides proboscideus, Mus mintoides, Desmodillus auricularis, Rhabdomys pumilio, Saccostomus campestris*. Two species of climbing rodents (*Rhabdomys pumilio, Saccostomus campestris*) captured in the ungrazed drainage line were absent from the grazed drainage line. Numbers of small mammals captured on the plains were similar for grazed and ungrazed land, but grazed plains were dominated by a single species of gerbil (*Gerbillurus paeba*) (Eccar et al. 2000). In Swaziland, South Africa, the distribution of small mammals were surveyed at 39 localities. A total of 15 species of rodents were captured during the survey, namely *Aethomys chrysophilus, Aethomys namaquensis, Dasymys incomtus, Leminiscomys rosalia, Mastomys pumilio, Thallomys paedulcus, Steatomys pratensis, Dendromus mesomelas, Dendromus mystacalis, Otomys angoniensis, Otomys irroratus, Saccostomus camperstris, Tatera leucogaster*. It was found that the number of rodent species captured was lower on

Swazi Nation Land compared with privately owned land or protected land. It was assumed that the phenomenons were due to radical habitat alteration, such as overgrazing, cultivation of maize and deforestation (Monadjem, 1999).

In Chile, South America, the effect of grazing by goats on species richness and abundance of rodents was also a mixed picture with density of some species (European rabbits) being higher while some species were lower (native rodents) (Simonetti, 1983).

By contrast, in several other studies, populations and/or species of small mammals were reported to increase on grazed sites.

In the Thar Desert, India, a research was done to compare the vegetation structure, rodent density and seed loss rate between protected and disturbed sites affected from grazing by cattle, goats and sheep. It was found that in the grazed site, plant coverage was low, but the density of rodent burrows and the frequency of rodent captures were significantly high as compared to the protected sites (Wada et al.1995). In New Mexico, desertification, a phenomenon partially due to overgrazing (Glantz and Orlovsky, 1983), was reported to have led to increased diversity and abundance of small mammals (Whitford, 1997).

It is noteworthy that the two papers by Johnson (1982) and by Reynolds et al.

(1980) did not specify or verify if the grazing was “overgrazing”. The paper by Monadjem (1999) did mention that “*at many of these Swazi Nation Land localities, not a single mammal was captured in the cattle grazing lands; instead all the small mammals were captured in abandoned maize fields*”, but it also failed to verify the existence of overgrazing on the Nation Land; instead, it was assumed there was overgrazing. One of the papers claimed to have the purpose to link *overgrazing* and small mammals in its title, but it actually studied relationship between grazing and small mammals (Wada et al.1995). Therefore, it seems that a correct assessment of the relationship between overgrazing and abundance of small mammals is still missing internationally.

3.2 Interaction between grazing practice and small mammal populations in China

In China, lack of systematic research in the past makes the issue unclear. With some fragmental records concerning small mammal populations and grazing practice, we could sort out a discrepancy between what is known and unknown on the issue.

It was recorded as early as 1964, in Luqu County, Gannan Tibetan Autonomous Prefecture of Gansu Province, herdsmen and farmers began to kill pika *(O. curzoniae)* at a large scale (Editorial group for General Situation in Gannan Tibetan Autonomous

Prefecture, 1987). In early 1970s, it was claimed that pika did a great harm onto pastures in Ruo’ergai County, Aba Tibetan and Qiang Autonomous Prefecture, Sichuan Province (Ruo’ergai County Editorial Commission for country record, 1996). In 1985 and 1987, small mammals (mainly *Myospalax baileyi*) were considered to be "*major pests of the pastures*" in Hongyuan County (Hongyuan County Editorial Commission for county record, 1996). After collectivization of livestock and pastures in late 1950s, Tibetan herdsmen in Shiqu County mainly stayed in winter pastures because they had no incentive to go to summer pastures, then the winter pastures were observed as overgrazed (Shiqu County Editorial Commission for county record, 2000). Meanwhile, small mammal outbreaks were not documented in Tibetan pastures in Rangtang County, Aba Tibetan and Qiang Autonomous Prefecture, Sichuan (Rangtang County Editorial Commission for country record, 1997). A recent research, which used vegetation indicators including “relative abundance of unpalatable plants”, “condition of palatable species”, “coverage of vegetation”, “relative degree of erosion”, and "relative abundance of colonizing species", suggested that in some parts of Tibetan pastures, the overgrazing might have happened centuries ago (Holzner and Krichbaum, 2000).

According to the Chinese Government Environmental Communiqué (Chinese

Environment Protection Bureau, 2001), in year 2000, there were about 400 million hectares of grassland that occupied about 40% of Chinese territory; Amongst these, 84.4% of the grassland areas were located in western China; It has become a common phenomenon in China in recent years that pastures are at serious risk of overgrazing, and the capacity of carrying livestock has subsequently decreased; In 2000, according to the communiqué by the Chinese Environment Protection Bureau, about 90% of the grassland in China was in the process of degradation and approximately 135 million hectares of grassland were seriously degraded, about 2 million hectares of pasture becoming seriously degraded each year; In parallel, population outbreaks of small mammals were recorded in rangeland in Sichuan, Qinghai, Gansu, Ninxia, Xinjiang and Inner Mongolia; In 2000, it was estimated that there were 28 million hectares of pasture that experienced small mammal outbreaks and it became to be considered as a '*disaster*' for 17.33 million hectares of pasture in the above provinces and autonomous regions in addition to other 6 provinces; the Communiqué did not mention how it concluded that the pastures were overgrazed and also it did not link overgrazing with outbreak of small mammals; However, it mentioned that overgrazing could be one factor promoting degradation of pastures (Chinese Government Environmental Communiqué, 2001).

Pikas have long been blamed for being responsible for degraded ranged lands on the Tibetan plateau (Smith and Foggin, 1999). Pastoralists usually attributed areas of degraded pasture to the activities of pikas (Ekvall, 1968; Formosov, 1928). It is a common habit to describe the degraded pastures as "mouse badlands or wastelands" (Li, 1995; Hou, 2001). Miller (1999) simply argued that overgrazing by livestock was a misconception; a general climatic trend to desiccation and warming might be responsible for vegetation changes in the alpine meadows of many parts of the Tibetan Plateau, however this author failed in giving information sources (Miller, 1999). Conversely, however, some believed that it was overgrazing that contributed to pastures degradation then to the outbreak of small mammals (Li, 1995; Hou, 2001). It was observed that pika could be found at higher densities on pastures grazed by yak, sheep and horses than on natural meadows (Shi, 1983; Zhang et al., 1998). Some believed that overgrazing had direct relationship with outbreak of small mammals, namely, overgrazing leading to pasture degradation then leading to small mammals invasion, then pastures further overgrazed by small mammals, then the pastures further degraded (Li, 1995; Hou, 2000). It was calculated that in Qinghai Province, the forage consumed by small mammals averaged 41.1 billion kilograms a year (Hou, 2000). However, although they admitted the scarcity of data, some others argued that the amount of forage consumed by pikas was negligible… (Holzner and Kriechbaum, 2001). In a more complex approach to link overgrazing and small mammals' outbreak, it is generally assumed in China that overgrazing, associated with climate changes and rodent invasion, leads to land degradation/desertification (Chen et al, 1998; Cheng et al, 1998; Wang G, et al., 2001).

When these references are further checked and analyzed, problems concerning the evidences used to justify the assessments and/or beliefs, and poor definition of key concepts, may be found. For example, Miller (1999) who claimed that overgrazing was a misconception, however failed to provide any definition of overgrazing and any concrete evidence to support his view; furthermore, concepts of "overgrazing", "privatization", or "traditional pastoralism" were often used without elaborating on their precise meanings in the papers. For the so-called "natural meadows" (Shi, 1983; Zhang et al., 1998), no exact definition could be found for this concept: in fact, as the Tibetan alpine pastures are open, they are all under graze by livestock… Furthermore, quantification of overgrazing is always vague in these papers. Therefore, it seems that, although the "overgrazing" concept has been widely used; it has been rarely or properly discussed or defined. In addition, it seems that in the above mentioned studies, few efforts were made to find ways to measure overgrazing. So we may well understand why the relationship between small mammal outbreaks and overgrazing that originates from economic arrangement has not been properly established yet.

In summary: 1) It appears that lack of methods to quantify overgrazing reliably is a problem through out the world; 2) the linkage between overgrazing and population density of small mammals is vague throughout the world and in China.

3.3 Partial fencing and AE prevalence in the Tibetan herdsmen communities

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Fenced pasture: A possible risk factor for human alveolar echinococcosis in Tibetan pastoral communities of Sichuan. ***Acta Tropica 90 (2004) 285–293.***

Abstract

Introduction

Materials and methods

Results

Discussion

Acknowledge

Reference

In summary for the paper: 1) Using multiple stepwise logistic regression, it was shown that partial fencing around the settlements in winter pasture was statistically significantly associated with the risk of human alveolar echinococcosis in the surveyed villages; 2) The underlying reason may lie in overgrazing, an assumed cause of population outbreaks of small mammal intermediate hosts of the parasite on the Tibetan plateau; 3) Overgrazing could have been exacerbated by the reduction of communal pastures nearby the settlements due to introduction of fencing around group tenure pastures acquired by Tibetan pastoralist families.

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Fenced pasture: a possible risk factor for human alveolar echinococcosis in Tibetan pastoralist communities of Sichuan, China

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Abstract

Alveolar echinococcosis, infection caused by the parasitic helminth *Echinococcus multilocularis*, is a zoonosis strongly linked to climatic and ecological factors. Cross-sectional survey data were used to test a hypothesis that partial fencing of pastures could promote alveolar echinococcosis transmission in semi-nomadic pastoral communities of the Tibetan plateau, PR China. Using multiple stepwise logistic regression with consideration of factors of age and gender, it was shown that partial fencing around the settlements in winter pasture was significantly and independently associated with the risk of human alveolar echinococcosis in the surveyed villages ($P = 0.021$). The underlying reason may lie in overgrazing, an assumed cause of population outbreaks of small mammal intermediate hosts of the parasite on the Tibetan plateau. Overgrazing may have been exacerbated by the reduction of communal pastures nearby the settlements due to introduction of partial fencing around group tenure pastures acquired by Tibetan pastoralist families.

Keywords: Alveolar echinococcosis; *Echinococcus multilocularis*; Fencing; Overgrazing; Tibetan herdsmen community; Risk assessment

1. Introduction

Echinococcosis is a major public health problem in western Sichuan Province, PR China, especially in the pastoral communities of the Tibetan plateau (Schantz

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et al., 1998; Qiu et al., 1999). Two types of echinococcosis, i.e. cystic echinococcosis (CE) and alveolar echinococcosis (AE) are known to be endemic in the area. Human AE, caused by the metacestode of the "fox tapeworm" *Echinococcus* (*E.*) *multilocularis*, is considered to be one of the most pathogenic and chronic parasitic zoonoses in temperate and arctic regions of the Northern Hemisphere (Eckert and Deplazes, 1999). Human CE, caused by the metacestode of the "dog tapeworm" *E. granulosus* has a cosmopolitan distribution and is also responsible for very significant morbidity in the area (Qiu et al., 1999). The intermediate animal hosts that harbour the larval stages of these two *Echinococcus* species and maintain the functioning of the parasite cycle in nature are, respectively, small mammals for *E. multilocularis*, and livestock for *E. granulosus*. In most endemic areas of China, domestic dogs also become infected and play a major role as definitive hosts of *E. multilocularis*, in addition to foxes (Schantz et al., 1998; Qiu et al., 1999). On the eastern Tibetan plateau, *E.multilocularis* larval infection was recorded in 25% (3/12) of plateau voles (*Microtus irene*) and in small lagomorphs [6.7% (5/75) of the black-lipped pika (*Ochotona curzoniae*) and 7.1% (1/14) of Tibetan hares (*Lepus oiostolus*)] (Qiu et al., 1999). Surveys for cystic echinococcosis in domestic livestock found prevalence rates of *E. granulosus* infection of 7.5%, in sheep (3/40) and 8.6% in yaks (66/766) (Qiu et al., 1999). Surveys of definitive hosts for adult tapeworm infection revealed *E. multilocularis* in 44.4% (76/171) of Tibetan foxes (*Vulpes ferrilata*) and in 12.1–25.0% (4/33–5/20) of stray dogs; adult-stage *E. granulosus* infection was also found in 21.2% (7/33) of stray dogs (Qiu et al., 1999). As determined in ultrasound mass surveys performed from 1997 to 1998, prevalence of AE and CE infection in humans in northwest Sichuan was 1.9% (76/3999) and 2.1% (84/3999), respectively (Qiu et al., 1999).

The local human population in Ganzi Prefecture, Sichuan consists mainly of Tibetans primarily engaged in livestock husbandry. Killing dogs is forbidden by Buddhism and this contributes to the permanent presence of a large number of stray dogs in the area. Epidemiological data thus indicate that environmental and social conditions are suitable for transmission of both AE and CE. Land use and spatial arrangement of habitats (i.e. "landscape factors") also appear to play a significant role in modifying the ecological conditions that favor the transmission of *E.multilocularis* in agricultural communities in northwest China (Giraudoux et al., 1996; Craig et al., 2000; Giraudoux et al., 2002). The population density of small mammals has been proposed to be a key factor for the transmission of *E.multilocularis*, high densities being significantly associated with infection of foxes and with the prevalence of AE in humans (Viel et al., 1999; Craig et al., 2000; Giraudoux et al., 2002). Reports of increased densities of small mammals, i.e. species of pika (*Ochotona curzoniae*), voles (*Microtus fuscus, Microtus Irene*), and mole rats (*Myospalax baileyi*) in degraded pastureland were assumed to be the result of overgrazing in areas of the eastern Tibetan plateau, principally in Sichuan and Qinghai Provinces where AE is endemic (Li, 1995; Hou, 2001). Since the 1980s, partial fencing around Tibetan pastoral settlements has become more common, in response to changes in land property regulations. This could have led to a decrease in the availability of communal pasture areas around the settlements, which in turn could have exacerbated the overgrazing situation. We thus hypothesized that partial fencing might play a contributory role in overgrazing, and consequently, to the increasing density of small mammals in non-fenced overgrazed areas close to the fenced settlements. If this hypothesis is correct, there should be an increased density of small mammal populations in those pastoral settlements with more partial fencing and consequently an increased prevalence of AE in humans in those fenced communities. This study therefore considers the possible linkage between partial fencing and the risk of human AE in Tibetan pastoral communities, with overgrazing considered as a possible factor influencing land use and consequent disease risk. Comparison of data on AE with those of the co-endemic CE, caused by *E. granulosus*, whose life cycle involves livestock rather than small mammal intermediate hosts, allowed us to better define possible confounding factors in a comprehensive approach to determine risk factors for human AE.

2. Materials and methods

From 2001 to 2002, an epidemiological investigation was conducted to determine the prevalence of human AE and CE in Shiqu County in northwest Sichuan

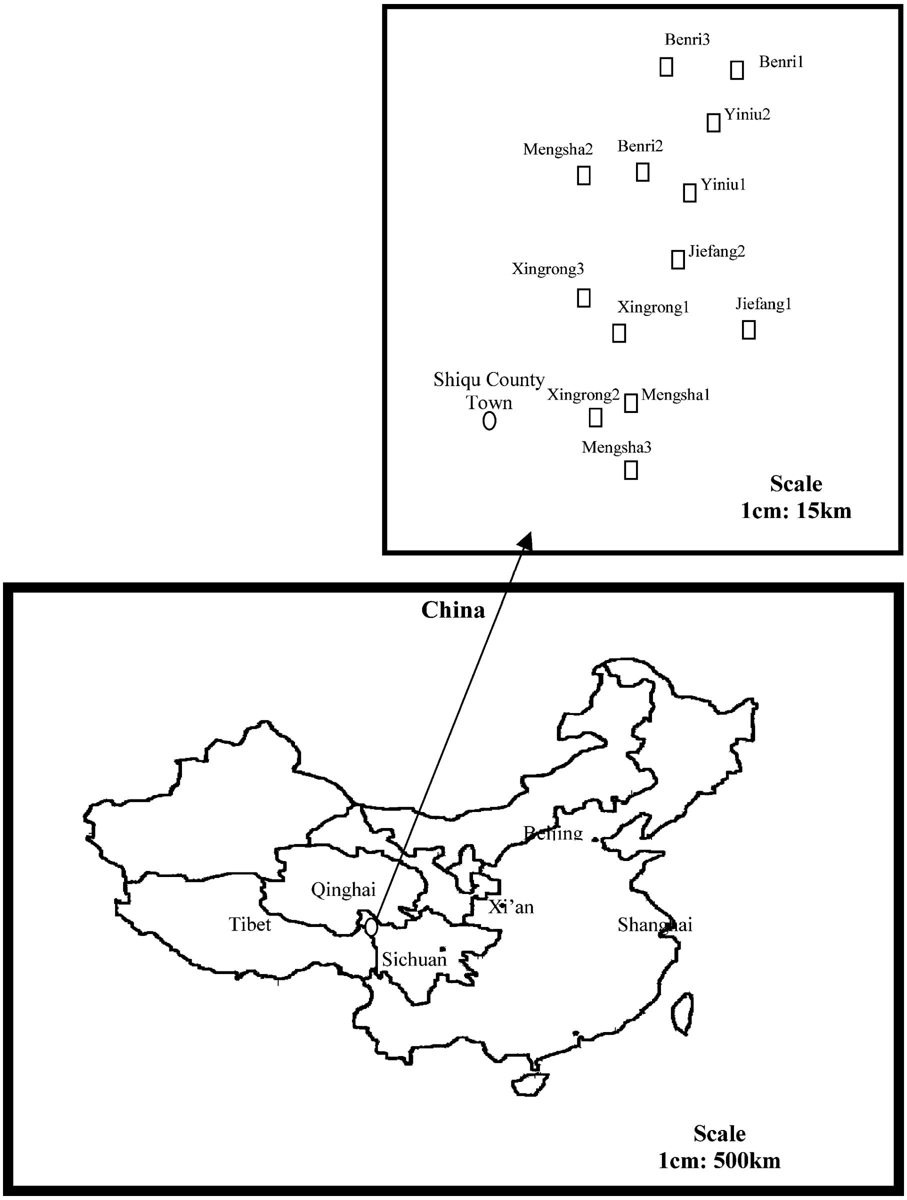

Fig. 1. The area investigated.

Province, China. One semi-urban area and eight livestock raising communities were selected as investigation sites. Selection of communities was based on the past records of the domicile areas of AE patients diagnosed on clinical symptoms and preliminary investigation of intermediate hosts in northwest Sichuan province.

2.1. Description of the study site

Shiqu County is located on the eastern Tibetan Plateau and is under the jurisdiction of Ganzi Tibetan Autonomous Prefecture, Sichuan Province (Fig. 1). The county is located at 97°20′00″–99°15′28″E and 32°19′28″–34°20′40″N. It shares a border with

Qinghai Province in the east, north and west and with the Tibet Autonomous Region in the south. Shiqu County covers an area of 25 100 km^2, with a mean elevation of 4200 m. Grassland covers an area of 21 000 km^2 of which 19 000 km^2 can be used as grazing pasture. Shiqu County consists mainly of three topographic areas—high mountains, high altitude meadows, and lower altitude grassland. The weather is affected by a monsoon climate and is characterized by wide temperature differences. Winter is longer than summer and frost conditions persist throughout the year. The humid season lasts from May to October. The mean annual rainfall is 596 mm. The average temperature is minus 1.6 °C (Editorial Commission of Shiqu County Record, 2000). In 1996, there were some 630 000 livestock that mainly consisted of yaks, sheep, goats, horses and a smaller number of pigs. The human population of this county was about 62 000 and 98% were ethnically Tibetan.

In Tibetan pastoral communities, the pastures are roughly divided into summer pastures and winter pastures. From October to next early May, the herdsmen stay in winter pasture settlements at 4100 m in average, comprising mud-brick houses and some tents and the livestock grazes on winter pasture in valley bottoms. From early or middle May to late September, the majority of livestock and people move to high altitude on valley slopes of the summers pasture at around 4300–4800 m where they live in tents. Fencing of winter pastures around the permanent winter settlements was initiated in 1986 (Editorial Commission of Shiqu County Record, 2000) in order to improve the productivity of the pasture. Tenure of open winter pastures is distributed to groups of individuals (group tenure), whereas the fenced areas of winter pasture are owned exclusively by individuals. Almost all winter pastureland is distributed to groups of herdsmen except for some pastures which belong to Buddhist monasteries and some pastures under the management of township government. The herdsmen collectively share the group tenure for the pasture and their houses are usually set up close to each other for security and mutual aid. The fencing is always erected nearby the house.

2.2. Data collection

Township officials and village cadres passed messages through herdsmen to inform the inhabitants where they could get free medical examination for echinococcosis. Voluntary self-selected subjects went to one of the designated screening places. Before examination, informed consent was obtained from all adult subjects and from the parents of minors. The study was approved by the Ethical Committee of Sichuan Institute of Parasitic Diseases, Sichuan Province as well as those of all collaborating investigators. After answering an epidemiological questionnaire, each registered person was given an abdominal examination using a portable ultrasound machine (SSC218, ALOKA Medical Equipment, Shanghai, China). Diagnosis was based on the ultrasound characteristics as recommended by the WHO-IWGE Ultrasound Classification scheme for echinococcosis (Vuitton and Pawlowski, 2001).

Access to fencing and pasture data was obtained through the cooperation of the local administration in every township. Data on the fenced properties of the surface area of pastures were obtained in two townships: Yiniu and Mengsha. In Yiniu Township, data were collected for its seven villages. In Mengsha Township, data were available for four of the six villages. The exact sizes of the fenced areas in each village were not available; however, village officials provided the data in terms of “bundles of pen”. One bundle of pen can fence an area of 3.75 mu (Chinese area unit,1 ha = 10 000 m^2 = 15 mu).

2.3. Statistical procedures

The overall goal of analysis was to test the hypothesis that partial fencing in villages could increase the risk of human AE. Therefore, the “estimated fenced area” in a village was selected for the analysis. The estimated fenced area in each village was the product of the number of bundles of pen and the area of pasture that one bundle of pen can fence.

The statistical procedures were conducted in three steps. In the first step, age- and gender-specific infection rates of the population under study were described and compared with Fisher Exact Test or Pearson Chi-square. In the second step, the estimated fenced area in village and the factors of age and gender were included as independent variables in a multiple stepwise logistic regression in which the dependent variable had two responses: the rest of the population and the AE patients. In the third step, a multiple stepwise logistic regression was fitted with independent variables of estimated fenced area in village and the factors of age and gender; the dependent variable had two responses: the rest of the population and the CE patients. SPSS release 10 was used to perform these statistical analyses.

3. Results

3.1. Population under study

The study population was entirely of the Tibetan ethnicity. The total population in the 11 villages was 4036 of which 17.5% (705/4036) were screened by abdominal ultrasound.

3.2. Infection rates of human AE and CE in the area under study

As determined by ultrasound screening, the prevalence of AE was 8.5% (60/705) and CE prevalence was 4.7% (33/705) in the population under study. AE prevalence was 7.1% (25/350) in males and 9.9% (35/355) in females. No statistically significant difference was found between the sex-specific prevalences (Fisher Test, two-tailed, $P = 0.225$). AE prevalence increased with age (PearsonChi-Square = 41.5, $P < 0.001$) (Table 1). The youngest person infected with AE was an 8-year-old boy and the oldest was a 77-year-old woman.

Table 1
Age specific infection rates of AE in Shiqu county, Sichuan, PR China

Age range	Number of people under study	Number of patients with AE	Infection prevalence (%)
1–11	136	1	0.7
12–23	147	2	1.4
24–34	145	12	8.3
35–51	141	23	16.3
52–86	136	22	16.2

3.3. AE infection rates and land-use situations in the villages under study

Table 2 shows the infection rates and land-use situations in each village. The total pasture area in the villages was 130 409 ha including 41 315 ha of winter pasture and 199 ha of fenced pasture inside the winter pasture. Among the villages, Mengsha2 village had the smallest fenced area (7.5 ha) and Jiefang2 village had the largest fenced area (28.7 ha).

3.4. Results of multiple logistic regression analysis

The factor “estimated fenced area in a village” was found to be significantly associated with prevalence of human AE, with age and gender taken into account. P value for the “fencing” factor was 0.021 and P value for the “age” factor was less than 0.001 (Table 3). P value for the “gender” factor was not statistically significant in the analysis ($P = 0.137$).

Table 2
AE infection rates and estimated fenced areas in the villages of Shiqu County, Sichuan, PR China

Township	Village	Number of people screened	Number of people with AE	AE infection rates (%)	Estimated fenced area (ha)
Yiniu	Benri1	87	6	6.9	18
	Benri2	81	5	6.2	17.3
	Benri3	52	3	5.8	10
	Yiniu1	125	14	11.2	22.5
	Yiniu2	98	9	9.2	23
	Jiefang1	65	6	9.2	24.5
	Jiefang2	80	12	15.0	28.7
Mengsha	Mengsha3	35	1	2.9	19.2
	Xinrong3	28	2	7.1	13
	Mengsha2	35	1	2.9	7.5
	Xinrong2	19	1	5.3	15.7

Table 3
Analysis of human AE transmission risk factors in Tibetan winter settlements using multiple stepwise logistic regression

Variables	Parameter estimate	Standard error	Wald	Degree of freedom	P	Odd ratio
Estimated fenced area in a village	0.062	0.027	5.300	1	0.021	1.064
Age	0.037	0.007	28.578	1	<0.001	1.037
Intercept	−5.057	0.661	58.515	1	<0.001	0.006

Significant risk factors.

Table 4
Analysis of human CE transmission risk factors in Tibetan winter settlements using multiple stepwise logistic regression; significant risk factors

Variables	Parameter estimate	Standard error	Wald	Degree of freedom	P	Odd ratio
Age	0.021	0.009	6.263	1	0.012	1.022
Intercept	−3.776	0.384	96.737	1	<0.001	0.023

In contrast, the prevalence of CE was not significantly associated with the factor "estimated fenced area in a village" ($P = 0.074$); increasing age was statistically significant ($P = 0.012$) (Table 4). Gender of those screened was not statistically significant ($P = 0.357$).

4. Discussion

The results of the study indicated that people living in villages with a greater area of fenced pasture had a significantly higher risk of infection with alveolar echinococcosis.

Estimation of fenced areas in these Tibetan communities relied on estimates of the quantity of fence used, i.e. bundles of pen purchased from agriculture administration in each community, and not on a precise measurement of the surface areas of fenced pastures. For a preliminary testing of the hypothesis, this indirect estimation appeared to be a practical indicator since, in these Tibetan pastoral communities, one village could be as extensive as 150 km^2, with no roads and it could take weeks, on horseback, to undertake the fencing measurement. It was observed that the behavior of herdsmen regarding fencing was quite similar in the various villages and that after the pen were purchased from township administrations, they were actually used for fencing. Cooperation of the township administrations was generally very good. When cooperation was not fully obtained (i.e. in 2 villages of Mengsha Township), the quantitative data on fencing were not included in the analysis. Evaluation of the prevalence of AE in this population can be considered quite reliable, since it was obtained by active mass screening using abdominal ultrasound examination. This approach for community screening of human AE in other parts of China has been shown to be highly effective and to give an accurate figure of the infection, both symptomatic and asymptomatic at a given time (Bartholomot et al., 2002).

The results of multiple stepwise logistic regressions, controlling for both age and gender as potentially confounding factors, confirmed that the estimated fenced area in a village was significantly associated with the AE prevalence in humans. The association between partial fencing and human AE prevalence may be related to ecological changes in land use that allow *E. multilocularis* to cycle more actively between potential definitive (Tibetan fox, red fox and dog) and intermediate hosts (especially *Ochotona* spp. and *Microtus* spp. in this area) within an otherwise homogeneous grassland environment. Partial fencing appears to serve as an indirect marker of overgrazing in winter pastures around settlements, because herdsmen may tend to fence more grassland around settlements where more forage is needed for the livestock; in addition, fencing could also exacerbate the grazing pressure on un-fenced, common pastures. In both situations, according to the hypothesis, our results suggest that small mammal abundance would be higher in villages with larger fenced areas than in those with smaller fenced areas. Population density of small mammals, especially those species whose population size follows a cyclical pattern have been shown to be associated with AE prevalence in humans (Viel et al., 1999). As partial fencing was initiated in the mid-1980s, the younger population should be more affected by the phenomenon, which might be manifested by higher infection rates among young age groups. Our data do not support this assumption, however (Tables 1 and 3). In order to show such differences this cross-sectional survey design may not be appropriate; data from a cohort investigation would be far better. It is unlikely that age-specific infection prevalence could reflect the influence of partial fencing on AE prevalence in young populations. AE is a chronic infection with a long asymptomatic stage, and its progression varies according to the individual immune response of the host (Vuitton et al., 2002). Mass abdominal screening using ultrasound detects virtually all existent cases irrespective of the date of exposure and cumulative exposure may lead to higher probability of infection for middle-aged and old people. Occupational and social behaviors in older age groups may also be involved in increasing risk of infection. In addition, overgrazing implies that the number of animals exceeds the productive capacity of the grazing land or pasture. Fencing was initiated in the 1980s because of changes in land property arrangements that were necessitated by extreme shortage of forage for livestock in winter (Editorial Commission of Shiqu County Record, 2000). It has been speculated that overgrazing was already serious before the 1980s, implying that prior overgrazing could have influenced both the abundance of small mammals and the perceived need for fencing and, consequently, lead to increased transmission of *E. multilocularis* infection for many years, including years before fencing, in some areas.

Several other factors, unrelated to ecological changes, may have contributed also to such a relationship. These include the age and the size of the settlements. For example, a village with larger fenced areas might have had a comparatively longer settlement history. A longer duration of settlement with or without fencing could have led to a comparatively poor general hygienic situation with increased fecal contamination by domestic dogs, and, consequently, a higher risk of AE for the community, irrespective of ecological changes. Poor hygiene may also be associated with larger numbers of households, hence a larger fenced area. If the above factors for the degree of transmission of *E. multilolcularis* to humans are valid then this should also apply to transmission of *E. granulosus* from dogs to humans. Statistical analysis, however, did not find a significant correlation between the area of fenced pastures in villages and the local prevalence of human CE. This suggests a direct link between AE and land use on the Tibetan plateau.

Previous risk factors described for *E. multilocularis* transmission to humans include the population size of definitive hosts (foxes, dogs, and cats) (Eckert and Deplazes, 1999; Petavy et al., 2000), landscape structures which lead to a heterogeneous distribution of infected foxes (Hansen et al., 2003), a history of dog ownership or contact (Craig et al., 2000), playing with dogs, lack of safe water source, age and gender, rearing of livestock (Wang et al., 2001), as well as the use of well water (Yamamoto et al., 2001). Dogs could play a key role in AE transmission due to their susceptibility to *E. multilocularis* and close association with humans in Tibetan pastoral communities. In such communities, dogs are usually tied up near the door of the house (or tent) in daytime and released in the night. Tibetan herdsmen usually tie up their livestock near their houses or tents during the night. Dogs are used to guard households day and night, and to drive away wild animals such as wolves, especially at night.

Landscape patterns have also been shown to be associated with high densities of rodents, and consequently to AE prevalence in endemic areas (Viel et al., 1999). Open landscapes with humid soil were suggested to be favorable for the life cycle of the parasite (Staubach et al., 2001). The proportion of grassland, scrub and shrub lands linked to deforestation patterns in Gansu, China has been shown to be significantly related to AE prevalence (Giraudoux et al., 1996; Craig et al., 2000). No previous studies have linked AE risk factors to the impact of livestock on the environment and particularly overgrazing. Relationships between overgrazing and small mammal populations is, however, a complex issue and remain poorly understood. In South Africa, overgrazing has been reported to lead to a decrease in the number of rodent species but the absolute number of rodents was not studied (Monadjem, 1999).

Conversely, in New Mexico, a study showed that desertification in fact led to species richness, increased diversity and abundance of small mammals (Whitford, 1997). It has been generally assumed in China that overgrazing, associated with climate changes, leads to land degradation/desertification (Chen and Liang, 1998; Cheng and Wang, 1998; Wang et al., 2001). It has also been argued that, although overgrazing by livestock is a key contributor to land degradation, in turn it could both be exacerbated by and contribute to small mammal invasions (Li, 1995; Hou, 2001). Overgrazing is a phenomenon usually believed to be favored by the existence of communal pastures in a community (Hardin, 1968) and it affects about 20% of the world's pasture and rangeland. Recent losses due to overgrazing have been most severe in Africa and Asia (FAO, 1996). According to the Chinese Government Environmental Communiqué for the year 2000 (General Bureau of National Environment protection, 2000), there were about 400 million hectares of grassland that occupied about 40% of Chinese territory and a big proportion was overgrazed. More than 80% of grasslands are located in western China where human AE is highly endemic (Wen et al., 2002). However, very few field studies have evaluated the effects of overgrazing on population outbreaks of small mammals or with partial fencing. The results of our current study strongly suggest that further research should be done on this issue especially in relation to transmission of *E.multilocularis* in parts of western and northwest China.

In conclusion, this preliminary study indicates that the degree of overgrazing, as quantified by the degree of fencing around communities in eastern Tibet was associated with an increased risk of human AE. The increased risk may be associated with increased populations of small mammals which act as reservoir hosts and whose populations increase on degraded pastures.

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3.4 Overgrazing and AE/*E.multilocularis* transmission

Qian Wang, ***Dominique A. Vuitton, Yongfu Xiao, Peter M. Schantz, Francis Raoul, Christine Budke, Wen Yang, Philip S. Craig, Patrick Giraudoux***

Socio-economic and ecological correlates of alveolar echinococcosis emergence in Tibetan pastoralist communities. ***Submitted to "Emerging Infectious Diseases".***

Abstract

Introduction

Materials and methods

Results

Discussion

Acknowledge

Reference

In summary for the paper: 1) open pastures were overgrazed comparing with fenced pastures; 2) In comparison to fenced pastures, the open pastures had higher burrow density of small mammals; 3) Higher overgrazing pressure measured by fenced area, led to higher burrow density of small mammals in the open pastures in all landscapes; 4) The median burrow density of small mammals in open pastures was independently associated with dog **E. multilocularis** ***infection; 5) Overgrazing appears to increase the density of small mammals, which may in turn promote maintenance and transmission of*** **E. multilocularis** ***in Tibetan pastoralist communities.***

Socio-economical and ecological correlates of alveolar echinococcosis emergence in Tibetan pastoralist communities

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Abstract

Alveolar echinococcosis, caused by *Echinococcus multilocularis,* is an emerging public health problem in Tibetan pastoralist communities. Grazing practices, small mammal indices and dog *Echinococcus multilocularis* infection data were used to test a hypothesis that overgrazing promotes *E.multilocularis* transmission through increasing populations of small mammal intermediate hosts. Analysis of grazing practices revealed that open (common) pastures were overgrazed comparing with fenced (private) pastures. In comparison to the fenced pastures, the open pastures had higher densities of small mammal burrows in valleys (p=0.005), valley entrances (p=0.005) and flatlands (p<0.001). Higher overgrazing pressure measured by fenced area, led to higher density of small mammal burrows in the open pastures in all landscapes: valley (r_s=0.382, p<0.001), flatland (r_s =0.312, p<0.001), piedmont (r_s=0.471, p<0.001) and valley entrance (r_s=0.296, p=0.001). The median density of small mammal burrows in open pastures was independently associated with dog *E.multilocularis* infection (p=0.003, OR=1.048). These results seem to support the hypothesis.

Article Summary Line: Overgrazing appears to increase the density of small mammals that may serve as reservoir hosts of the parasite, which may in turn promote maintenance and transmission of *E. multilocularis* in the Tibetan pastoralist communities.

Human alveolar echinococcosis (AE) is an infection caused by *Echinococcus (E.) multilocularis*, a highly pathogenic zoonotic cestode with a life cycle involving foxes as definitive hosts (hosts of the adult stage) and small mammals as intermediate hosts (hosts of the larval stage, or metacestode). Human AE, albeit restricted to localized endemic areas is of public health concern in central Europe (1). It has become a major public health problem in western China (2, 3) where dogs have been shown to act as definitive hosts (4, 5). Mass ultrasound surveys in Tibetan communities of Sichuan province, PR China, in 1997-1998, documented a high prevalence of AE in humans, averaging 1.9% (77/3998) in the population (4), and 2.3% (43/1858) in the subpopulation engaged in livestock raising, 97.0% of whom were Tibetans (6). In more recent surveys, the prevalence was as high as 8.5% in Tibetan pastoralist communities (60/705) (7).

Since the 1980s, partial fencing of pastures around Tibetan pastoral winter settlements has become common as a result of changes in land property regulations (8). The fenced areas are primarily used to provide forage for weak, young or pregnant livestock during winter and early spring when forage is extremely limited. This may lead to significantly less livestock grazing pressure on the privately-owned fenced areas than in community-owned open pastures. In addition, partial fencing reduces the area of community-owned open pastures and this, consequently, may increase grazing pressure on the open pastures. Thus, it might be hypothesized that proportionately larger fenced (private) areas create higher grazing pressure on the open (communal) pastures. In a previous work we could show that, in these communities, the extent of fenced pastures was positively related to human AE prevalence (7). We suggested that the reason could be an increase in the density of small mammal intermediate hosts of the parasite, due to exacerbated overgrazing in open pastures by partial fencing leading to higher level of infection in community dogs, then higher contamination pressure on humans in their environment (7).

However, the relationship between grazing and small mammal populations is a very complex phenomenon which remains poorly understood. Livestock grazing was reported to affect small mammal populations negatively in both richness and abundance in sagebrush rangeland of Idaho, USA (9) and in South Africa (10). In contrast, populations of small mammals were shown to increase on grazed sites in the Thar Desert, India (11). In the Great Salt Desert, the USA, heavy grazing produced a mixed picture with the densities of some species increased, while the densities of the others decreased (12,13). On the Tibetan plateau, some have suggested that when combined grazing of yak, sheep and horses lowered the height of vegetation, *Ochotona(O.) curzoniae* might be found at greater densities than on natural meadows (14,15). It was assumed that overgrazing led to outbreaks of small mammals including plateau pika (*Ochotona curzoniae*), mole rats [*Myospalax(M.) baileyi*] and voles [*Microtus (M.) fuscus, M. irene*] (16,17). However, it has also been argued that the lowered grass could be the result of *O. curzoniae* invasion (18,19). In this area, as in other ones in the world, the actual link between overgrazing and density of small mammals is thus not clearly understood.

The existence of both fenced (private) pastures and open (communal) pastures in an otherwise homogenous environment provided us with a unique opportunity to investigate the effect of overgrazing on the abundance of small mammals in the Tibetan pastoral winter settlements and its potential consequence to contamination pressure by infectious agents which depend on small mammals as a reservoir host. With this goal 1) we studied livestock management practices in both fenced and open pastures as well as herdsmen’s perceptions of scarcity of forage in winter and early spring; 2) we compared the densities of small mammal burrows, as an indicator of their population density, in fenced pastures and in open pastures; 3) we determined the relationship between the density of small mammal burrows in the open pastures and the surface of fenced pastures, and 4) we studied the relationship between the median density of small mammal burrows in open pastures and dog infection with *E. multilocularis* in winter settlements.

Materials and Methods

Site description.

The study was carried out in 3 townships in Shiqu County of Ganzi Tibetan Autonomous Prefecture in northwest Sichuan Province, China, in spring and autumn 2003. The selection of the investigation sites was based on documented high prevalence of AE in humans by mass screening, and the observation of a variety of fencing practices in the area (7).

Shiqu County is located on the eastern Tibetan Plateau at 97°20'00"-- 99°15'28"E and 32°19'28"-- 34°20'40"N, has a population of 62,000 (98% ethnically Tibetan), and shares a border with Qinghai Province in the east, north and west and with the Tibet Autonomous Region in the south. It covers an area of 25,100 km^2, at a mean elevation of 4,200 m, 19,000 km^2 of which can be used as grazing pasture. The weather is affected by monsoon climate, with a mean yearly rainfall of 596mm, and is characterized by wide temperature differences (average temperature -1.6 C°). Winter is longer than summer and frost conditions persist throughout the year (8). In 1996, the livestock population was about 630,000 and consisted of yaks, sheep, goats, horses and a small number of pigs.

Data collection

The study was approved by the Ethical Committee of Sichuan Institute of Parasitic Diseases, Sichuan Province as well as those of all collaborating investigators. The investigation was performed in 30 settlements of 3 Tibetan pastoral townships (18 villages). If a settlement was located in a narrow valley (less than 1 km width), the landscape was described as “valley”; if located in the entrance to a valley, it was described as “valley entrance”; if located at the foot of a hill and facing a flat land on the other side, it was described as “piedmont”; if located in a wide valley (more than 1 km with a flat bottom), it was described as “flat land”.

A questionnaire was administered to the herdsmen after obtaining individual informed consent. In small settlements (less than 10 households), all households with herders at home were investigated. In large settlements (equal to or more than 10 households), a random selection of 10 households in settlements with less than 20 households but more than ten, or half the households in settlements with more than 20 households was investigated. The questionnaire covered demographic information, number of livestock, livestock management practices and herdsmen's perception of the discrepancy between needed forage and the productivity of the winter pasture.

For each settlement, whenever possible, the surface of fenced pastures was measured using a GPS (GPS 12, Garmin International Inc., USA). Small mammal populations were monitored using index methods. These methods are based on the detection of surface indicators of small mammals, i.e. holes and feces (20,21,22,23), and are usually employed to link small mammal indices and habitats on a large scale (24,25). Sampling was performed by 2 investigators walking at approximately 1 km per 1.5 hours along a 1 km transect drawn across each settlement. Along this transect, 50 counts of small mammal burrows were performed; each count covered an area 20 meters long and 10 meters wide (about 200m^2). For valley, valley entrance and piedmont settlements, transects began at a point 20 meters to the right of the first house in the direction of entrance into the settlement. If it was impossible to walk in this direction (for example, facing a very steep hill), the starting point changed to the left of the first house. For settlements on flatland, transects went north beginning from a point 20 meters away from the northernmost house of the settlement.

In settlements where transects were done in 2 townships, all dogs were sampled through arecoline purgation, according to the recommendations of OIE/WHO (26), and/or collecting ground feces when accessible and available (5). Purgation and feces samples were taken to the Sichuan Institute of Parasitic Diseases (SIPD) in Chengdu, where helminths were removed, counted, and placed in 10% formal saline or 85%

ethanol. Species identification of worms was done at SIPD, and copro-PCR testing at the School of Environmental and Life Sciences, University of Salford (UK), using species-specific primers for *E. multilocularis* DNA amplification based on the method of Dinkel et al (27) as modified by van der Giessen et al (28).

Statistical analysis

Data related to livestock management, perception of the gap between the forage needs of livestock and the production capacity of the pastures, the density of small mammal burrows, the area of fenced pastures and prevalence of dog infection in settlements were used in the analysis. Landscape was taken into consideration for the analysis because the potential productivity could vary among pastures with different landscapes.

The density of small mammal burrows outside fenced areas was compared with that within the fenced areas using non-parametric tests considering landscape factor. Spearman correlation tests were used to quantify the relationship between the density of small mammals outside fenced areas and the surface of fenced areas in settlements where the fenced areas were all measured, also controlling the landscape factor. Multiple stepwise logistic regression was used to relate median density of small mammal burrows to dog infection in the settlements. The dependent variable was *E. multilocularis* positive (0) or not (1). Independent variables included dog age and sex, "ground collected fecal samples" vs. "purged fecal samples”, as well as median density of small mammal burrows. All these analyses used SPSS release 10.

Results

The Qiwu, Yiniu, and Xiazha townships (populations 2,238, 2,515, and 2,471, respectively) covered 1,046 km^2, 955 km^2, and 834 km^2, respectively. Herders from 128 households were interviewed and a total of 30 km of transect were walked over 30 settlements. Areas of fenced pastures were all measured in 22 settlements and purged feces or/and ground faeces were collected from 252 dogs in 15 settlements in Yiniu and Xiazha townships.

1. Livestock management

In these Tibetan pastoralist communities, almost all the population was engaged in raising livestock. The average number of persons per household was 4.57 (SD=1.76). Average livestock populations included 26.1 yaks (SD=17.9), 11.1 sheep or goats (SD=27.0), and 1.4 horses (SD=1.7) per household. Among the 128 households, 92 (71.9%) owned fenced pastures; 2 households borrowed fenced pastures; 94 households allowed their livestock to graze inside the fenced area in wintertime. Usually, by May, the herders moved their livestock to summer pastures. Most herdsmen (87.2%, 82/94) only allowed young, old, sick and pregnant livestock to graze in the fenced pastures, while the rest permitted all their livestock to graze inside the fenced pastures. A total of 69.5% (89/128) of the investigated herders reported that available forage could not satisfy the needs of their livestock in winter pasture; 27.3% (35/128) thought that the available forage was extremely deficient during winter months while 3.9% (5/128) had no idea on this issue.

2. Characteristics of the settlements

The average number of households in a settlement was 8.3 (SD=6.2). The smallest settlement had 3 households and the largest had 25. The average surface of fenced pastures per settlement, calculated from data of 22 settlements where the surface of all fenced pastures could be measured, was 49,915.9 m^2. The enumeration of small mammal burrows based on 1,500 observations was done along the 30 km of transect. Some fenced pastures (13%, 24 of 186 measured fenced pastures) were also shared pastures. However, only 5 among these 24 fenced pastures were owned collectively by 4 to 7 households. One transect inside the fenced area was done in a shared fenced pasture that was owned by 4 households and 2 of the 3 owners surveyed indicated that all their livestock were permitted to graze inside this fenced area from February / March to May. This fenced area was actually used communally, and consequently, overgrazed. Therefore, the transect data in this settlement was not included in the following analyses.

3. **Distribution of small mammal burrows**

The distribution for small mammal burrows was highly skewed. Kolmogorov-Smirnov test indicated that both in fenced pastures ($p<0.001$) and outside fenced pastures ($p<0.001$), the data did not fit a normal distribution. Normality was not obtained after Box-Cox transformations.

Overall, landscape type influenced the abundance of small mammal burrows ($P<0.001$). Post-hoc Tukey multiple comparison test on ranks confirmed that the densities of small mammal burrows were different among different landscape types ($p<0.05$) (except for the comparison between flatland and piedmont, $p>0.05$). The density of small mammal burrows in open (common overgrazed) pasture was greater than that in fenced (private non-overgrazed) areas (p <0.001). Table 1 shows that the densities of small mammal burrows in open pastures were significantly higher than these in fenced pastures in 3 of all 4 landscapes.

The Spearman correlations found that the bigger fenced areas led to higher density of small mammal burrows in the open pasture in all landscape types, namely valley (r_s=0.382, p<0.001), flatland (r_s=0.312, p<0.001), piedmont (r_s =0.471, p<0.001) and valley entrance (r_s=0.296, p=0.001) (Table 2). The relationships between the area of fenced pastures and the density of small mammal burrows inside the fenced pastures in the 4 landscapes, were not significant except for flatland [valley (r_s=-0.079, p=0.322), flatland (r_s=-0.458, p=0.024), piedmont (statistics not applicable due to 3 observations only) and valley entrance (r_s=0.081, p=0.736)].

5. **Relationship between median densities of small mammal burrows in open pastures and *E. multilocularis* infections in dogs**.

In total 252 dogs were sampled for feces, of which 159 (63.1%) were purged in 15 settlements. Based on coproPCR testing, overall the dog *E. multilocularis* infection rate was calculated to be 16.7% (42/252) for the 252 dogs (183 males /252; mean age 4.41yrs); the infection rate for purged samples was 18.2% (29/159); and the figure for ground collected faecal samples was 14.0% (13/93). Multiple forward conditional stepwise logistic regressions showed that the median density of small mammal burrows in the open pastures was significantly positively related to dog infection (p=0.003, OR=1.048) (table 3). Dog age (p=0.524) and sex (p=0.782) as well as the nature of the sample, i.e. ground sample vs. purged sample (p=0.380), were not found significant.

Discussion

Increased densities of small mammal populations in open pastures and their association with dog infection were the "missing link" that was needed to confirm our hypothesis of a relationship between overgrazing and the prevalence of human AE suggested in a previous study (7). The data obtained in the current study seem to provide evidence for such a link and confirmed the socio-economical and ecological correlates of the emergence of alveolar echinococcosis in pastoral communities of the eastern Tibetan plateau.

The role of overgrazing on small mammal population dynamics is one factor that has not been adequately documented. Grazing and “overgrazing” might have different consequences and evaluating this phenomenon could allow us to better understand the transmission of small mammal-born diseases to humans. Overgrazing is a problem that may be caused by human behavior and the arrangement of property rights of pastures. From an ecological point of view, overgrazing is a process caused by herbivores leading to a continuous decrease of pasture productivity over time. According to Hardin (29), overgrazing is the result of overstocking of communal pastures; and occurs under two conditions: 1) livestock raising is a key industry in the community where pastures are scarce resource; 2) the existence of communal pastures. The Tibetan pastoralist communities investigated had both these features. Considering that current practice of most herders permitted only "weak" livestock to graze inside the fenced pasture in winter and early spring, one can assume that the fenced pastures were generally well protected and not overgrazed. In contrast, open pastures experienced unlimited grazing by all livestock so that vegetation was often severely degraded. Hence, the comparison between open winter pastures and fenced winter pastures was actually a comparison between “overgrazed” and “balanced" or "non-overgrazed" pastures.

On the eastern Tibetan plateau, the plateau "pika", *O. curzoniae* (*avra*, in Tibetan) was the most commonly observed small mammal and this observation was also supported by several other surveys (16, 8, 30). These small lagomorphs live in large colonies and their burrows are easily seen as they occur mostly in open pastures with low vegetation cover, and are noticeably associated with degraded pastures, often leading to bare ground. It has been estimated that one hectare of Tibetan alpine pasture corresponded to 2,600 pika burrows, equivalent to 273 *Ochotona curzoniae* (31). In this area, however, there were several potential intermediate hosts for *E. multilocularis*, including *O. curzoniae, O. cansus, Cricetulus kamensis, Microtus. leucurus, M. irene, and M. oeconomus/limnophilus* (30). Biases could have been introduced when counting the burrows of small mammals inside fenced pasture because of the high grass resulting from the lower grazing pressure. In our survey, fenced pastures were located on the slopes, bogs, flatlands, and riverbanks, and the species of small mammals within the fenced pastures also included voles of *Microtus* spp(*amazi* in Tibetan) and pika of *Ochotona* spp. In fenced grassland with high grass, the most common small mammal, however, was *M. oeconomus/limnophilus* (30) whose burrows are typically small and round (about 3 cm diameter). The grass around the burrows of *Microtus* spp was obviously lower and conspicuous runways were also evident, therefore, their burrows were usually visible. The mole-rat, *Myospalax baileyi* (*xielong* in Tibetan), was also reported to be a prominent pasture resident on the Tibetan plateau (16, 17) However, we found only a few burrows of this rodent species which builds large size “molehills” (diameter: about 25 cm) and surrounded by short vegetation. Among the 6 species identified in this area, several species were trapped within similar habitats (e.g. *O. curzoniae*, *O. cansus* and *Cricetulus kamensis* in overgrazed pastures) (30), making the use of small mammal surface indices particularly important. The “burrow” index should thus be taken as a crude and global estimate of the population relative density of the small mammal community (likely including the genera *Ochotona*, *Microtus* and *Cricetulus*, depending on the habitats).

The current study revealed that a greater proportion of fencing was associated with a higher density of small mammal burrows and the higher median density of small mammals was linked to a significantly higher prevalence of *E.multilocularis* coproPCR positive dogs in the Tibetan communities investigated. In a previous study, using multiple stepwise logistic regression with consideration of patient age and gender, it was shown that partial fencing around Tibetan settlements in winter pasture was significantly and independently associated with the risk of human alveolar echinococcosis in surveyed villages (p = 0.021) (7). We assumed that partial fencing could increase overgrazing in the open pastures and consequently increase indices of the species related to risk of AE transmission to humans in those communities (7).

The current study appears to support the hypothesis that partial fencing is able to increase populations of potentially susceptible small mammal species in open pastures, especially the pika *O. curzoniae*, which is a recognised intermediate host of *E. multilocularis* on the eastern Tibetan Plateau (3,4). A previous study indicated that *E. multilocularis* prevalence in *O. curzoniae* was 6.7% (5/75) in the same study area (4). The population density of small mammals seems to be one of the key factors for the transmission of *E.multilocularis* in other studies because high densities were found quantitatively associated with infection of red foxes and human AE in France or in Gansu (China) (32, 33, 34, 35). Our data seem to support these observations in a Tibetan pastoral area, where dogs are probably an important definitive host of *E. multilocularis* (4, 5). Thus we consider the overgrazing on the eastern Tibetan plateau to constitute a potential risk for increased exposure to human AE infection amongst pastoral groups.

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Biographical Sketch

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Table 1. Comparisons of densities of small mammal burrows in open pastures with these in fenced pastures stratified by landscapes (Density: number of burrows per 200 m^2 of pasture)

		No. Of observations	Mean rank of densities	Sum of ranks of densities	Mann-Whitney U	Z	Asymp. P (2-tailed)
Valley	Open pastures	616	439.07	270464.50	63715.500	-2.784	0.005
	Fenced pastures	234	389.79	91210.50			
Flatland	Open pastures	175	109.38	19141.00	634.000	-5.819	<0.001
	Fenced pastures	25	38.36	959.00			
Piedmont	Open pastures	155	96.91	15020.50	2930.500	-1.643	0.100
	Fenced pastures	45	112.88	5079.50			
Valley entrance	Open pastures	180	103.83	18690.00	1200.000	-2.833	0.005
	Fenced pastures	20	70.50	1410.00			

Table 2. Relationship between surface of fenced pastures and densities of small mammal burrows in the open pastures in the settlements (Spearman correlations)

In open pasture	Valley	Flat land	Piedmont	Valley entrance
No. of observations	490	126	147	130
Correlation Coefficient	0.382	0.312	0.471	0.296
P (2-tailed)	<0.001	<0.001	<0.001	0.001

Table 3. Relationship between median density of small mammal burrows in open pastures and dog *E. multilocularis* infections in the settlements.

	Parameter estimate	Standard error	Wald	df	P	Odds Ratio
Median of small mammal burrows	0.047	0.016	8.924	1	0.003	1.048
Constant	1.089	0.224	23.705	1	<0.001	2.971

Dog sex and age as well as the nature of the fecal samples (“ground sample" vs. "purged sample”) were not found significant by the multiple forward conditional stepwise logistic regression

Chapter 4 General discussion

Guiding questions: 1) what are the risk factors for AE prevalence in the Tibetan pastoralist communities? 2) How does overgrazing influence the transmission of AE/E.multilocularis? 3) What are the difficulties in measuring overgrazing and what are the solutions? 4) What should be further done to understand how much the overgrazing hypothesis could be applicable?

4.1 Summary of the results

This study evaluated a series of socioeconomic and behavior factors as potential risk factors for AE transmission with a focus on overgrazing and its causes to be a possible risk factor promoting the populations of small mammal intermediate hosts of *E.multilocularis* that could in turn facilitate transmission of *E.multilocularis* in a Tibetan pastoralist region.

From the analyses of risk factors concerning socioeconomic and behavioral aspects, it was revealed that increasing age for all communities, and “non-preventing flies from food” in herdsmen communities, “residence in Shiqu County”, “number of dogs kept” and “ownership of fox skin” in farmers’ communities, “female gender”, “drinking water from streams” and “playing with dogs” in urban communities could be important risk factors of AE for the respective populations. Most of the disclosed risk factors focused on a major role for dogs in *E. multilocularis* transmission in the studied communities, as previously did several studies in other parts of China. However, in addition, a direct role for foxes in *E.multilocularis* transmission to humans was pointed out for the first time in China by our epidemiological study.

For the first time too, in the Tibetan pastoralist communities, the existence of overgrazing and its possible indirect consequence on human health was confirmed by using a socio-economical paradigm combined with an ecological approach. Our research revealed that in open pastures, unlimited grazing by livestock was permitted. By contrast, the fenced pastures were well managed in terms of timing of grazing and limiting livestock access.

In fact, on one hand, partial fencing around the settlements in winter pasture was found to be significantly and independently associated with the risk of human alveolar echinococcosis in the surveyed villages (p=0.021) by a multiple stepwise logistic regression with consideration of factors of age and gender. On the other hand, in comparison to fenced pastures (not overgrazed), the open pastures (overgrazed) had a higher density of small mammal burrows in valleys (p=0.005), valley entrances (p=0.005) and flatlands (p<0.001); Spearman correlations analyses found that the larger fenced area, associated with higher overgrazing pressure, led to higher density of small mammals' burrows in the open pasture in all landscape types, namely valley (r_s=0.382, p<0.001), flatland (r_s =0.312, p<0.001), piedmont (r_s=0.471, p<0.001) and valley entrance (r_s=0.296, p=0.001).

Pasture management system is likely the main reason for the difference between fenced pastures and open pastures because the pastures are nearby and under the same climate situation and presumably under the same threat of invasion by small mammals. Overgrazing was exacerbated by partial fencing of pastures that further promoted overstocking of livestock on the commons that were otherwise reduced in size as a consequence of fencing.

The median density of small mammal burrows in open pastures was revealed to be independently associated with dog infection by *E.multilocularis* (p=0.003, OR=1.048) by a multiple stepwise logistic regression analysis considering dog sex and age as well as the type of measurement of dog infection. This observation, on the Tibetan plateau further confirmed that dogs might play an important role in AE/*E.multilocularis* transmission as was also found in other Chinese provinces such as Gansu (Craig et al, 2000). In addition, dogs were found to play a role in *E.multilocularis* transmission to human by risk factors analyses.

Discussions focused on the data obtained in every individual study are given in each of the 3 original papers published or submitted. The following general discussion will especially deal with the methodological issue of the definition and measurement of overgrazing, and will try to give a synthetic view of the interference between intrinsic, environmental and behavioral factors in the occurrence of AE in a given region/community, with special reference to the Tibetan plateau.

4.2 Evaluation and/or measurement of overgrazing: difficulties and debates

At the beginning of our work, we felt the difficulty to define, describe and quantify "overgrazing". Reviewing the literature concerning the relationship between overgrazing and small mammal densities, it seems that we face several problems: 1) lack of definition of overgrazing in the past researches that tried to relate overgrazing to small mammal density; 2) lack of proper measurable indicators of current (as well as past) overgrazing. Some ecological indicators were suggested to measure the consequences of overgrazing, for examples, change in plant cover, in plant species, animal densities and species etc. (USDA 1937, Costello and Schwan 1946, Weaver 1968, Stubbendieck et al 1986, Holechek et al. 1989, Fleischner 1994). Animal indicators may include changes in small mammal species and densities. For example, in Tibetan alpine pastures, pika is viewed as an indicator of overgrazing (Shi, 1983; Zhang et al., 1998; Hou, 2001; Li, 1995). However, it may be argued that such changes in pika density might not be the outcome of overgrazing, but of temperature and humidity changes, and could even be the reason for vegetation changes and thus "overgrazed" aspect of the meadows (Chen et al, 1998; Cheng et al, 1998; Wang G, et al., 2001; Miller, 1999). Therefore, because of this somehow "vicious circle", it seemed that ecological indicators or livestock husbandry indicators were not readily applicable to our research.

After checking available possibilities, we turned to socio-economics indicators that seemed to be more reliable given the socio-economics origin of overgrazing. Through the definition of overgrazing in terms of socio-economics paradigm, two indicators were adopted to verify the existence of overgrazing: 1) scarcity of pastures and 2) common ownership of pastures. By questionnaire investigation, we successfully identified these two features in the surveyed Tibetan communities and even indirectly measured the overgrazing pressure, which enabled us to further understand the relationship between overgrazing and density of small mammals.

4.3 Small mammal communities and their role as reservoir of *E. multilocularis*

Being the intermediate hosts of *E.multilocularis*, small mammals play a key role as reservoir of *E.multilocularis*. But for different species, their role can be very different and actually depends on 3 main factors: 1) their respective susceptibility to

E.multilocularis infection; 2) their population densities; 3) the contact opportunities of these small mammals with the faeces of carnivore definitive hosts, such as foxes, dogs and cats (Zhou HX, 2001).

The population density of small mammals seems to be one of the key factors for the transmission of *E.multilocularis*: high densities were found quantitatively associated with infection of foxes and with the prevalence of AE in humans in France and Gansu Province, China (Viel et al., 1999; Craig et al., 2000; Giraudoux et al 2002; Giraudoux et al. 2003). However, in some areas, such as Switzerland and the USA, occurrence of human AE cases was not found related to the prevalence in intermediate and/or definitive host (Bruno et al., 2001; Hildreth et al., 2000). These studies will be given in more detail below, since they also pointed out that environmental factors and behavioral factors, at a society scale, were mixed to give the final picture and favor *E. multilocularis* transmission, permanently or temporarily, in a given area.

In Tibetan pastures, the situation of small mammals is far from clear in terms of all above 3 factors listed above. From data obtained by field trapping of small mammals, visual observation and literature review, 18 species of small mammals belonging to 10 genera have been described in the area we worked in. They are: *Lepus oiostolus, Ochotona curzoniae, Ochotona cansus, Ochotona gloveri, Ochotona* *thibetana, Cricetulus longicaudatus, Cricetulus migratorius, Cricetulus kamensis, Microtus fuscus, Microtus oeconomus, Myospalax baileyi, Apodemus chevrius, Apodemus agrarius, Apodemus peninsulae, Rattus norvegicus, Niviventer confucianus, Marmota himalaya,* and *Eozapus setchuanus* (Chen, et al., 2001). Not all species of small mammals are fully identified, their distribution patterns and densities were not studied systematically, and their susceptibilities to *E. multilocularis* infection were not systematically investigated in the region.

E.multilocularis larval infection was recorded in 25% (3/12) of voles (*Microtus irene*) and in lagomorphs [6.7% (5/75) of the black-lipped pika (*Ochotona curzoniae*) and 7.1% (1/14) of Tibetan hares (*Lepus oiostolus*)] (Qiu et al., 1999). Most of *Microtus* sp. and *Ochotona curzoniae* are very susceptible hosts to *E. multilocularis* which may acquire fertility in these hosts and thus make the cycle function efficiently. The role of the hares as a good intermediate host is most debatable. *E.multilocularis* infection in dogs and foxes was quite high, the infection rate was calculated to be 18% for owned dogs based on copro-PCR testing (Budke et al, 2005); the figure for stray dogs was 12.1-25.0% (4/33-5/20) and 44.4% (76/171) for Tibetan foxes (*Vulpes ferrilata*) (Qiu et al., 1999). Therefore, the transmission cycle between small mammal intermediate hosts and their carnivore definitive hosts seems to work quite well. The positive relationship we found between density of small mammal burrows and *E.multilocularis* infection in dogs confirmed the current interaction between intermediate and definitive hosts in our area of research. However, the correlation was found between dogs and small mammal indices in the "open" "common" pastures, i.e. presumably mostly due to the presence of *Ochotona* sp., but a role for the small mammals (mostly rodents/voles) present in the "fenced" "private" pastures cannot be ruled out. In fact *Microtus spp* like to live in areas with high grass, and their presence has been demonstrated by trapping and transects in the same area (Raoul et al, manuscript under submission). We may suppose that carnivores might not easily find them since they may hide in high grass; their role as reservoir could thus be hampered. These voles have however been often recognized as major intermediate hosts in a variety of biotopes worldwide (Viel et al, 1999; Giraudoux et al, 2003; Craig et al, 2003) and they cannot be neglected when the issue of the "most relevant intermediate host" on the Tibetan Plateau is discussed. A role for other types of potential intermediate hosts, for example, *Myospalax baileyi*, a kind of rodent, of comparatively large size, which was also depicted as a major species among the small mammals on the Tibetan plateau (Li, 1995; Hou, 2001) is also possible. Its accessibility by dogs and foxes might be impaired by its underground life, consequently its role as reservoir of *E.multilocularis* would be limited except if individuals trapped for crop protection were given to dogs. So, although *Ochotona* sp. are good candidates and seem to be favored as relevant intermediate hosts in the area of our study, its actual responsibility and a potential role for other suitable hosts remain to be confirmed by further researches.

4.4 Environmental, intrinsic and behavioral factors for AE transmission

Epidemiology of human alveolar echinococcosis (AE) is complex (Craig, 2003), and endemicity in a given area depends on a number of factors which may interfere to give the final issue, i.e. AE prevalence in humans. Environmental and behavioral factors have been the main epidemiology research focuses because they are the keys for mapping out control strategies (Vuitton et al, 2003; Craig et al, 2003; Eckert and Deplazes, 2004). The genetic and immunological approach to better understand AE epidemiology is more recent (Vuitton, 2003; Eckert and Deplazes, 2004). AE prevalence in a community depends on the main following factors. (1) Presence of susceptible definitive hosts (primarily dogs and foxes). (2) Presence of populations of susceptible mammalian intermediate hosts (small mammal species). (3) Occurrence of environmental features that enable egg survival prior to ingestion by intermediate hosts. (4) Maintenance of environmental conditions that provide optimal habitats for small mammals. (5) Biotic potential of the parasite itself. (6) Genetic and immunological characteristics leading to susceptibility/resistance in intermediate and definitive mammalian hosts. (7) Presence of socio-cultural features conducive or not to domestic animal involvement (especially dogs). (8) Behavioral characteristics that may lead to increased man-dog contact and/or to increased contacts with wild carnivores. (9) Socio-economical behaviors of the community, and/or political decisions at a higher level, that may lead to increase the parasitic reservoir in nature (intermediate and definitive hosts and their interplay) (Vuitton et al, 2003; Craig et al, 1996; Macpherson & Craig, 2000; Eckert and Deplazes, 2004). Transmission risk factors are usually tracked within the above 9 points. "Environmental factors" can be described as external factors that contribute to the functioning of the transmission cycle, which therefore cover the above 1st, 2nd, 3rd, and 4th points. "Intrinsic factors" that are genetically associated with characteristics of the parasite and its hosts may be assigned to the 5th and 6th points. The so-called "behavioral factors" are included into the 7th, 8th and 9th categories. It may be stressed, however, that socio-economic and/or community behavior factors may interfere strongly with environmental factors, and this especially constitutes the 9th point.

4.4.1 Environmental factors

(1) Presence of susceptible definitive hosts

Foxes, from different species, are usually considered to be the main (often even the only) definitive host for *E. multilocularis* (Craig et al, 2003; Eckert and Deplazes, 2004). This is the reason given to explain the usually "rural" foci of the disease in humans, since contacts with foxes are limited by occupational and/or specific behavioral factors. On the Tibetan plateau, several species of foxes are present and may act as reservoir for *E. multilocularis.* Among wild animals acting as definitive hosts, wolves, present too on the Tibetan plateau may also be involved (Zhang 1997, and personal observations). In Europe, growing populations of foxes and their increasing immigration to urban areas are new risk factors (Eckert et al 1999). In Germany and Switzerland, urban foxes have been found infected and this could be a new threat to urban populations (Romig, 2002;). However, domestic animals may also be involved. In France, in North of Alps and South of Jura, around the Swiss town of Geneva, the cestode *E. multilocularis* was found in three out of 81 domestic cats necropsied given by veterinarians; In an endemic area of alveolar hydatid disease, the prevalence of *E. multilocularis* in the domestic cat confirms that it is could be a risk factor for human beings and mainly for veterinarians (Petavy et al., 2000). Among risk factors studies in another European endemic area, Austria, in a limited series of human cases, owning cats was found to be a significant risk factor (Kreidl et al, 1998). However, fertility of *E. multilocularis* in domestic cats has often being considered to be low, and the actual role of cats in the parasitic cycle is doubtful (Thompson et al, 2003). In North America, besides foxes, village dogs were considered important in the spreading of the parasite to human communities (Rausch & Fay, 2002). In Gansu Province, China, questionnaire analysis indicated that total number of dogs owned over a period was a risk factor (P<0.006), but not a history of red fox hunting (P>0.6) (Craig et al., 2000; Giraudoux et al. 1996). In a research done in Tibetan communities of Qinghai Province, dog care was found to be statistically significant for AE prevalence by univariate analysis; among the 1445 settled participants, allowing dogs to sleep indoors was statistically significant (Schantz et al, 2003). In Tibetan communities of Sichuan Province, China, dogs were found to be positively associated with human AE prevalence (Wang et al., 2001).

Conversely, some other researches found no relationship between some definitive hosts and AE prevalence. In Switzerland, high prevalence of *E.multilocularis* in domestic animals (dogs and cats) seemed not to be associated with a higher clinical AE incidence in humans living in the same region (Bruno et al., 2001). In South Dakota, the United States, no association was found between higher prevalence of *E.multilocularis* in wild canid and deaths in trappers (Hildreth et al., 2000).

In our risk factor analysis, the number of dogs kept (p=0.022, OR=1.722) and ownership of fox skin (p=0.017, OR=6.583) in farmers' communities were found associated with AE infection; for urban population, people actively playing with dogs had a higher risk than persons who claimed never playing with dogs (p<0.004, OR=4.550). However, in the herdsmen communities, where the number of owned and stray dogs was enormous and the foxes population assumed to be bigger, the "dog factor" (number of dogs kept, dogs kept by neighbors, playing with dogs) and "fox factor" (owning fox skin products) were not found significant. We may assume that it is because the environment of herdsmen communities was heavily contaminated, so that the presence of dogs and/or fox products and interaction with dogs were covered by other factor, such as "not-preventing flies from access to food".

(2) Presence of populations of susceptible mammalian intermediate hosts (small mammal species)

In France it was shown that human AE was strongly influenced by the densities of arvicolid species (Viel et al., 1999). In Gansu Province, China, small mammal ecology studies revealed an association between density indices of voles (*Microtus* *limnophilus*) and village AE prevalence rates (Craig et al., 2000; Giraudoux et al. 1996, 2003). In Switzerland, however, it was documented that from spring 1993 to spring 1998, the prevalence of *E.multilocularis* in rodents was 9% to 39% for *Arvicola terrestris* and 10% to 21% for *Microtus arvalis*. However, high prevalence of *E.multilocularis* in wild (*Arvicola terrestris and Microtus arvalis*) seemed not to be associated with a higher prevalence of AE in humans living in the same region (Bruno et al., 2001). Another example is on the St Lawrence Island of Alaska. A large population of *Clethrionomys rufocanus* was found with high *E.multilocularis* infection but was not considered to be important for *E.multilocularis* transmission because the animal was not vulnerable to arctic foxes, the main wild definitive host in the region (Rausch, 1995).

Our research showed that the areas under study had a high density of small mammals, high *E.multilocularis* infection in owned dogs and high human AE prevalence rates. Furthermore, we revealed that in the Tibetan communities, the density of small mammals in open pastures was positively related to the *E.multilocularis* infection in dogs, which was a statistically significant risk factor for human AE prevalence. The issue of the actually involved species has already been discussed above: involvement of rodent species present in fenced pastures should be more precisely studied before any conclusion can be accurately given on this issue.

(3) Occurrence of environmental features that enable egg survival prior to ingestion by intermediate hosts

Eggs of *E.multilocularis* remain infective for approximately 1 year in a suitable, moist environment at lower temperatures, but they are sensitive to desiccation and high temperatures (Viet et al, 1995). Their high resistance to low temperature is a condition for their survival in Arctic regions. These eggs can survive at -50°C for 24 hours but are killed at -70°C with 96 hours and at -80°C within 48 hours (Eckert and Deplazes, 2004). Deep-freezing at -70°C for tat least 4 days or at -80°C for at least 2 days is recommended for inactivating *E.multilocularis* eggs in carcasses or intestines of final hosts or in faecal material before examination in the laboratory (Eckert et al., 2001).

In Shiqu County, the yearly average temperature is –1.6C° (Shiqu County Editorial Committee for Shiqu County Record, 2000). Temperature in January, when herdsmen are in winter pastures, averages -12°C and may reach -25°C. These temperatures are quite suitable for the survival of eggs. Temperature in July, at the altitude level of the winter pasture and of the summer pastures averages 7.7°C and 9°C and may reach 18°C and 20°C respectively, and thus theoretically allows the eggs to be inactivated during the summer season. Eggs may, however, be protected from heat and desiccation, especially when the soil is tramped by cattle and horses, as was shown in other endemic areas (Delattre, et al, 1998, 1990; Giraudoux et al, 2002); this may often happen on the Tibetan plateau. In addition, the very high densities of small mammals in the study areas presumably make the chance of ingestion of eggs before inactivating quite high.

(4) Maintenance of environmental conditions that provide optimal habitats for small mammals

Landscape patterns have been shown to be associated with high densities of rodents, and consequently to AE prevalence in endemic areas. The population dynamics of mammalian species is influenced by landscape (Giraudoux et al, 2003). Cyclic high densities of rodents was found to be significantly associated with permanent grassland in France (Viel et al., 2000) and with scrub and shrub lands in southern Gansu, in PR China (Giraudoux et al, 1998, 2003). One way to conceptualize this with respect to arvicolid rodent multi-annual cycles is the ROMPA hypothesis (Lidicker, 1985, 1988, 2000; Ostfeld, 1992). ROMPA refers to the ratio of optimal to marginal patch areas and is most frequently expressed as the proportion of a landscape composed of optimal habitat for the target species. The ROMPA could influence the probability that arvicolid population densities would undergo multi-annual cycles as a combined effect of dispersal and predation. If optimal habitats were scarce (low ROMPA), then the landscape matrix would serve as a large dispersal sink and population densities would be very stable and small. At very high ratios, rodent densities would also be stable but relatively large (vole dispersal occurs within optimal habitats and sink area, and predation is not enough to reduce population density). At intermediate ROMPA, multiannual rodent population cycles would be more likely (Lidicker, 1995; Hansson, 2002). Thus the average density of arvicolid population would tend to be described by a non-loner function of the ROMPA. Furthermore, mammalian predator-prey relationships appear to change with the relative proportion of the most productive habitats in heterogeneous landscapes (Angelstam et al, 1984; Oksanen, 1990; Hansson, 1995). It was concluded that the ecology of potential small mammal intermediate hosts, which included landscape quantification and consideration of ROMPA might be an important approach in the study of transmission of small mammal-borne zoonoses at regional scale such as alveolar echinococcosis (Giraudoux et al, 2003).

Grassland is an optimal habitat for small mammal species involved in *E.multilocularis* transmission comparing with forest and ploughed fields (Giraudoux et al, 2003). In our study areas, the landscape is almost homogenous: grassland only. Our research indicated that in this environment, overgrazed pasture could be a more optimal habitat for some species. Using the ROMPA concept in this area would be highly valuable to understand if the ROMPA hypothesis holds on the Tibetan Plateau.

4.4.2 Intrinsic factors

(1) Biotic potential of the parasite itself

Potential pathogens to humans or animals differ in their biotic potential. For instance, *T. hydatigena* and *T. ovis* have high biotic potentials with the production of large numbers of eggs and large numbers of metacestode cysts developing in sheep. In contrast, the biotic potential of *E.granulosus* was described as relatively low, representing less than 5% of the potentials of *T. hydatigena* and *T. ovis* (Gemmell and Roberts, 1998; Eckert and Deplazes, 2004).

A research in our study area found that mean intensity of infection (the mean number of parasites per infected host) with *E. granulosus* was 959 worms, with a mean intensity of 1084 worms for *E. multilocularis* infection (Budke et al, 2005). It could thus be suggested that the *E. granulosus* and *E. multilocularis* had similar biotic potential in the definitive host assuming other things being equal. As the definitive hosts have a balanced opportunity to be infected by both *Echinococcus spp*, comparison of CE and AE prevalence in the communities appears thus fully justified

To remain infective before ingestion by small mammals is also a key component for biotic potential. As evoked above, environmental temperature and humidity influence egg survival and infectivity but do not regulate the parasite population (Eckert and Deplazes, 2004).

In addition to the biotic potential linked to the number of worms present in the intestine of the final host and of eggs dispersed in the environment, genetic characteristic of the parasite species may participate in the infectivity of the hosts by the parasite. Until recently *E. multilocularis* was considered to be a very homogeneous species, with no genetic differences between isolates in different areas and even in different parts of the world (Craig et al, 2003). Using microsatellite DNA markers, this homogeneity is now questioned (Bart, thesis). These new molecular tools should be applied to the parasites circulating on the Tibetan plateau. Recently too, on morphological and molecular grounds, a new species of *Echinococcus*, different from *E. multilocularis*, was disclosed in animal hosts and has been proposed to be named "*Echinococcus shiquicus*" (Xiao et al., 2005). Its actual potential as a pathogen for humans and its role, different from or similar to *E. multilocularis* or *E. granulosus* in human diseases should be taken into account in further mass screenings.

(2) Genetic and immunological characteristics leading to susceptibility/resistance in intermediate and definitive mammalian hosts.

Resistance and susceptibility of mammalian hosts may influence either the optimal functioning of the parasitic cycle or the transmission to humans.

Species differences in the susceptibility of rodents towards *E.multilocularis* larval growth was stressed long ago, and served as a basis for the classification of intermediate hosts (Rausch, 1986). Most inbred strains of mice are susceptible, especially AKR, Balb C, C57 Bl6, among those which have commonly been used as experimental models of AE (1). C57 Bl 10 mice have usually been found relatively resistant (Hill, 1998; Liance et al, 1990; Bresson-Hadni et al; Gottstein et al 1994); however, when studied in congenic C57 Bl 10 mice, immune responses and cytokine secretion have not unequivocally been related to the H2 background of mice (Emery et al, 1997). Outbred NMRI mice are among the most resistant experimental hosts, and a comparison of NMRI and the highly susceptible AKR mice has shown that resistance was associated with the intensity and development of fibrosis which is itself immunologically mediated (Guerret et al, 1998). The genetic and/or immunological reasons for the susceptibility of some but not all carnivore hosts to the development of the worms in the intestine are far less known. Composition of the bile, able or not to favor protoscolex transformation into worms has been evoked long ago (Romig and Bilger, personal communication) but no other factors have been clearly related to susceptibility or resistance of definitive host. Resistance/susceptibility of the various species of intermediate hosts determines fertility of the larval stage; resistance/susceptibility of the various species of definitive hosts determines fertility of the adult stage. This has to be taken into account in echinococcosis when considering the role of a given species of intermediate host in the transmission of the larva to definitive hosts, and that of definitive hosts in the transmission of oncospheres to humans, thus when planning for control. In endemic areas, various species of potential intermediate hosts of *Echinococcus* species are usually present, as disclosed by veterinary studies (for livestock) and/or by trapping or hunting (for wild animals); however only fertile larvae, with protoscoleces, can infect carnivores. Relatively resistant hosts may be easily infected but maintain the larvae at a non-fertile stage. This observation especially applies to the Tibetan plateau, where the number of potential intermediate hosts is high, their habitats different (open versus fenced pastures, for instance) and their actual respective infectious potency for definitive hosts largely unknown.

Although the relationship between genes of the Major Histocompatibility Complex (MHC) and resistance/susceptibility in mice could not be demonstrated (Emery et al., 1997; Vuitton DA, 2003), a significant link between MHC polymorphism and clinical presentations of AE has been shown (Vuitton DA, 2003). A European study with 150 AE patients has shown a significant association between HLA DR 11 and protection, HLA DPB1*0401 and susceptibility, and HLA DR3 and DQ2 and severe clinical evolution of the disease (Eiermann et al., 1998). Studies on cytokine secretion by PBMC from HLA DR3+, DQ2+ patients with AE compared with patients without this HLA haplotype have shown that the spontaneous secretion of IL-10 observed in all patients with a progressive AE was much higher in these patient with HLA DR3+, DQ2+ (Godot et al, 2000). AE cases observed in central China were shown to be associated with HLA DR4, but no immunological correlates have been reported in this population of patients (Li Furong et al., 2000). Other genes within the MHC were also shown to be involved, such as the MHC class 1 Transport-Associated Protein (TAP) gene (homozygote Thr-Thr form of the TAP2 665 codon site) (Vuitton DA, 2003).

Clustering of AE cases in an extended family of a single Hui village in Ningxia was recently shown; as risk factors were quite similar in this village where AE prevalence averaged 5% in the community, and where CE cases were not clustered in a particular family, a genetic susceptibility to the infection is highly probable (Yang, PhD Thesis, 2005). A limited number of family cases have been observed in an endemic area of France (Pelletier et al., 2000); preliminary data indicate that relatives with progressive forms of *E. multilocularis* infection shared both HLA haplotypes and the associated clinical presentation of the disease (Pelletier et al., 2000). However, genetic "resistance" was evoked to explain the absence of human cases in an area where rodent infection by *E. multilocularis* was particularly high (Gottstein et al., 2001).

In the area we studied, nearly all infected subjects belonged to the Tibetan ethnic group, which is quite homogeneous in this area, with no mixing with the Han population or other ethnic groups. We cannot exclude, however, that some families may have shared "susceptibility genes" that could explain their particular sensitivity or resistance. A detailed analysis of case clustering could be done in this particular ethnic situation.

4.4.3 Behavioral factors

(1) Presence of socio-cultural features conducive or not to domestic animal involvement (especially dogs)

It has been assumed that the presence of dogs in Eskimo communities in Saint Laurence island was an important factor for the maintenance of the parasitic cycle close to the houses; in this part of the world dogs were used in the past for transport but sedentarisation increased the number of stray dogs roaming around the settlements, and feeding on rodents (Rausch et al, 2002). In China, presence of dogs in the villages was considered to be an important cause of the high prevalence of AE in Gansu (Craig et al, 2000; Wang et al, 2001) and in Ningxia (Yang, PhD thesis, 2005); they were cared by women and this was an explanation for the higher number of females than males among AE patients, as was found in our screened populations. In both areas, however, in the past 10 years, killing rodents using poisoned baits eventually killed the majority of dogs; this could in turn decrease AE transmission in these areas (Giraudoux et al., 2003; Yang, PhD thesis, 2005). This example shows that human behavior, even indirectly, may influence the number of definitive hosts and their contacts with human populations and thus, by chance, interfere with transmission.

Keeping dogs is very popular in the study areas. Culture in the Tibetan communities is also very conducive to the existence of large number of dogs. Tibetan people mostly believe in Buddhism, which makes them refuse or very reluctant to kill any kind of lives. Besides, the dogs serve as security guards for the families and livestock. Tibetan people bring redundant dogs to temples and towns, where people or Tibetan Buddhist/Lama would feed the dogs and the dogs could have more access to food. The number of dogs in the Tibetan communities actually depends on the availability of food. Therefore, the number of dogs is almost always at its highest-level possible; this is particularly true in herdsmen communities. Our risk factors research revealed that the "dog" factor was statistically significant in farmer and urban communities. Dogs likely play a very important role in herdsmen communities too, but their omnipresence might not allow the analysis to discriminate between families and communities.

(2) Behavioral characteristics that may lead to increased man-dog contact and/or to increased contacts with wild carnivores

Many behaviors could directly or indirectly increase man-dog contact and /or contract with wild carnivores. In Japan, multivariate analyses indicated that the rearing of cattle and pigs and the use of well water were significant risk factors and that the use of tap water significantly decreased the risk for an individual to get AE. (Yamamoto, et al., 2001). In Xinjiang Uygur Autonomous Region, factors including ethnic groups, eco-geographical zones and sex were found statistically significant using univariate analyses (Zhou et al., 2000). In a research done in Tibetan communities of Qinghai Province, the significant univariate factors for echinococcal infection (both CE and AE) included livestock ownership, Tibetan ethnicity, female gender, low income, herding occupation, limited education, water source, age greater than 25 years old, poor hygienic practices, offal disposal practices and dog care. Multivariate analysis revealed that livestock ownership was a significant risk factor for both forms of the disease, as well as age greater than 25 years, female gender, herding occupation, and being nomadic (vs semi-nomadic or settled). Being female and being older than 25 years of age were significant factors among the 1,906 semi-nomadic participants. Among the 1,445 settled participants, allowing dogs to sleep indoors was statistically significant (Schantz et al, 2003). In Tibetan communities of Sichuan Province, a number of AE risk factors were found statistically significant by single factor analyses in a research which included age, economic region (herdsmen region, urban region and agriculture region), education and occupation (Qiu et al, 2000). In another study on livestock raising populations in the same region, univariate analyses also found a number of statistically significant AE risk factors including sex, age, nomadic life style, drinking water sources, preventing flies from food and playing with dogs; In multivariate analyses it revealed that only age and playing with dogs to be statistically significant risk for AE prevalence (Wang et al, 2001).

In the study region, it is a common behavior for herdsmen to tie the dogs to the door way or in the front of tents. The dogs defecate just around the house or tent, which forms an assumable highly contaminated environment. In fact, owned dogs were proved to have high *E.multilocularis* infection (Budke et al, 2005). In our risk factor analysis, “playing with dogs” was found to be a risk factor for AE prevalence in urban communities. From the questionnaire and personal observation, we may assume that in Tibetan communities, humans have very close contacts with dogs. It was observed when people were getting close to house or tent, the owner of dogs was usually asked to “qia rong”, which means “hold the dog”, and the owner or his family members (usually the women) would do it in a very adroit manner that indicated a very close relationship between local people and their dogs.

Tibetan people do not use chopstick or cutlery to eat. They usually carry their food to their mouth with their hands and/or a knife. As was mentioned above, the most common dish is the Zhanba, which is prepared with the fingers and the palm of the hand. Water is scarce and washing hands may not be too frequent…These common behaviors also increase the contact between food and dog feces. The specific issue of female gender high risk has been thoroughly discussed in the relevant paper on "risk factors". Their proximity to dogs, their role in preparing food, and their handling of yak feces possibly contaminated by infectious dog feces, are all specific behavioral factors that make women at higher risk than men to be contaminated in Tibetan communities.

(3) Socio-economical behaviors of the community, and/or political decisions at a higher level, that may lead to increase the parasitic reservoir in nature (intermediate and definitive hosts and their interplay).

Socio-economical behaviors of the community, and/or political decisions at a higher level could be conducive to create an ecological environment for the thriving of small mammals in AE/*E.multilocularis* endemic areas, which may in turn promote *E.multilocularis* transmission. In France, it has been shown that agriculture policy change in 1960s led farmers to specialize in milk production and convert ploughed fields into permanent grassland, which caused an increase in the amplitude of the pluriannual density fluctuations of water vole in the Doubs Department (Giraudoux et al, 1997). The density of water vole (*Arvicola terrestris scherman*), as mentioned above, was linked to human AE prevalence (Viel, 1999). In Gansu Province, China, it was suggested that, in the area, long-term transmission of *Echinococcus multilocularis* and risk of zoonotic infection of south Gansu farmers might be related ultimately to a process of deforestation driven by agriculture. This in turn probably resulted in the creation of optimal peri-domestic habitats for rodents that serve as intermediate host species (such as *M. limnophilus*) and subsequent development of a peri-domestic cycle involving dogs (Craig et al., 2000; Giraudoux et al. 1996; 2003). In this area, AE risk was strongly associated with the presence of key microtine rodent species that were prone to seasonal and/or pluriannual population fluctuations within agriculturally fragmented upland landscapes (Giraudoux et al. 1996, 1998).

In our research, we linked grazing practice to an environment change that consequently was conducive to higher density of small mammals, which might in turn promote *E.multilocularis* transmission among dogs and consequently might increase the prevalence of human AE. Grazing practice is however, deeply influenced by property rights arrangement of the pastures, which has being heavily discussed in the parts of “2.1 Definition of overgrazing and origin of overgrazing” and “2.2 Property rights and grazing practices: history and current aspects”. The differences found between AE prevalence in farmers in Shiqu and Ganzi counties, partially relating to fox skin products owned, could also be linked to environmental changes in Ganzi county, favored by human activities, i.e. the extension of ploughed fields and deforestation which seems to have occurred earlier in this county.

4.5 Open questions

Our research succeeded in establishing a relationship between overgrazing and an ecological indicator, namely, the burrow density of small mammals. In 3 landscapes, namely, valley, piedmont and flatland, it was revealed that the burrow density of small mammals was higher on open pastures than that on fenced pastures. However, there was no significant difference between the two kinds of pastures in landscape of valley entrance. In the analysis of data, one transect was excluded because the fenced pastures on which transect was done was used in common by several families. This particular situation was observed while we were doing the fieldwork. It is quite possible that some other pastures on which transects were done were also used in common by several households, and that this fact was not recognized when we did transects. This could be a factor that influences the results in landscape of valley entrance.

Data including year of fencing and number of owners as well as the relationship among owners should be further considered to understand the situation. If the year of fencing is very close the time of survey, there might be no difference between two kinds of pastures. Also, if too many households own the fenced pastures, or agree upon using them in common without any special regulation, it makes the fenced pastures more close to commons. However, if these households have a good cooperation, for example, if among these households there is an obvious chief who can enforce regulations to protect the fenced pastures, the results could be very different. Including these additional factors would make the statistical analyses more meaningful, nevertheless more complex. The distribution of data on small mammals was detected as extremely far from normal distribution. Moreover, the data distribution seems to fit a so-called "zero-inflated distribution", which asks for “zero inflated” Poisson model to fit multiple factors models.

In this investigation we performed detailed studies in a small part of winter pastures only. If overgrazing in winter pastures around the settlements contributes to abundance of small mammals that may in turn promote transmission of AE, further understanding of the overall overgrazing situation in both winter pastures and more extensive summer pastures should also be obtained since the Tibetan families live in both environments. We privileged winter pastures since it appeared that closest contacts with potential *E. multilocularis*-transmitting definitive hosts might occur in winter, and that the recent presence of fenced pastures would likely more influence land use of winter pastures than that of summer pastures which are far from organized settlements. In summer pastures, households in tents are more isolated and each surrounded by a greater extent of pastures. However, overgrazing is also present in summer pastures and high densities of small mammals were also observed, and contamination of humans in summer pastures cannot be ruled out totally.

The research did indirectly link overgrazing to *E.multilocularis* transmission to dogs and AE prevalence in human. Can we directly establish a causal link between overgrazing and human AE prevalence? This may be done based on a direct measurement of overgrazing which asks for a methodology development of quantification of overgrazing. This should also be associated with a quantitative direct assessment of small mammal species in the various habitants, which requires systematic trapping and identification in the same areas.

4.6 Conclusion and perspectives

The major conclusions of this study are the followings: 1) significant risk factors for Tibetan communities in Sichuan Province include the number of dogs kept, playing with dogs, allowing fly contact with food, ownership of fox skin, female gender, and drinking water from streams; 2) overgrazing does promote high population density of small mammals that facilitates *E.multilocularis* transmission to dogs; 3) such an active functioning of the parasitic cycle, favored by overgrazing of common pastures, is likely the reason for the significant correlation between partial fencing of pastures in winter settlements and AE prevalence in the studied community.

Our research showed that overgrazing increased on communal pastures together with the increase in partial fencing, which means that the productivity of communal pastures decreased meanwhile. It could be presumed that if a village was overgrazed, the livestock would have less and less forage and, consequently, this could lead herdsmen to find a solution to forage shortage. This trend could generate a vicious cycle given a relatively stable number of livestock. In fact, it may be figured out that, as overgrazing intensifies, there is less forage output from the winter communal pastures which then leads to fencing more pastures to provide forage for weak animals to survive during hard seasons; the more fencing would then reduce the communal winter pastures more and more. Consequently, there could be continued and sustained overgrazing, which might lead to continuously increasing abundance of small mammals, both in common and fenced pastures, conducive to increasing transmission of AE before the pastures totally destroyed which makes the land not suitable for the survival of livestock as well as humans…In Mengge 1 village and Mengge 2 village, Mengyi Township, Shiqu County, the number of livestock kept per capita decreased from 10.3 in 1984 to 2.3 in 1993; in 1995, 64 households (243 people) had no longer livestock at all; and 95% of pastures in the two villages had become what is usually called "black beaches" (rodent wasteland) (Li, 1995). During field works in 2003, we observed that more fencing was being done in these communities, which seems to justify our hypothesis. Thus, further research and follow-up monitoring is necessary to further understand the trend.

Another prospective direction could also add knowledge to the issue of overgrazing and transmission of AE/*E.multilocularis*. As Hardin (1968) suggested, the existence of communal pasture is the main reason of overgrazing. Would elimination of communal pasture be able to decrease or eliminate overgrazing and thus finally decrease transmission of *E. multilocularis* in the Tibetan plateau? A prospective experiment could serve to find an answer. Alternatively, common organization of common pasture use has proved to be efficient in other countries and/or cultures, for example commons in middle altitude plateau in Franche-Comté, France, or in mountain alpine pastures in Switzerland, by limiting the number of livestock and organizing their land use to forage, and by sharing the ultimate product of cow breeding, cheese made from their milk.

Another open question is the potential extrapolation of the overgrazing hypothesis to other Tibetan pastoralist communities. According to personal observations, that would need further documented studies, overgrazing leads to at least two final results concerning the population density of small mammals, which might be highly species-sensitive: 1) In Shiqu County, overgrazing leads to an increasing density of small mammals of the *Ochotona*.spp, which are active on the surface of ground and lead, according to our current research results and literature data, to a higher level AE/*E.multilocularis* transmission. 2) In Hongyuan County, higher density of small mammals was also reported but the species was *Myospalax baileyi*, the predominant species of small mammal of this region, underground small mammals (Hongyuan County Editorial Commission for county record, 1996) that are supposedly not very accessible to foxes, dogs and cats. A population outbreak of this species was also reported in Shiqu, Sichuan Province and Qinghai Province and was suggested to be the result of overgrazing (Li, 1995; Hou, 1997). However, the prevalence of AE in the Hongyuan County is very low. On the other hand, *Myospalax* spp. in many other Chinese Provinces and Autonomous regions seems particularly associated with ploughed fields and agriculture, in areas where few livestock is raised and very little grassland is left (Giraudoux et al, 2002). Therefore, appropriate studies in areas like Hongyuan County where AE prevalence is very low, on the actual links between overgrazing and outbreaks of small mammal populations would be very useful to better understand overgrazing linkage with AE/*E.multilocularis* transmission.

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ANNEX

【论著】

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Investigation of Risk Factors for Development of Human Hydatidosis Among Households Raising Livestock in Tibetan Areas of Western Sichuan Province

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【Abstract】 **Objective** To identify factors influencing the development of hydatidosis in Tibetan areas of western Sichuan. **Methods** A questionnaire investigation was carried out to collect data on factors related to hydatidosis among households raising livestock. **Results** Analyses of data revealed that dogs rather than foxes were the most important source of AE transmission. People below 19 years old tended to suffering from CE rather than AE and people 19-38 years old, especially the females, were under an increasing risk of suffering from AE (female vs. male, OR=2.438, CI=1.317-4.514, $P<0.05$). Increased risks of both AE and CE prevalence associated with nomadic life, aging, playing with dogs, not protecting food from flies, and raising yaks or sheep. **Conclusion** In addition to age, sex, environmental conditions and hygienic behaviors, raising yaks or sheep and playing with dogs also increase the risk of suffering from hydatidosis as well in this area.

【Key words】 hydatidosis, risk factor, investigation

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四川省西部藏区家庭饲养牲畜人群包虫病风险因素的调查

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【摘要】 目的 寻找四川省西部藏区家庭饲养牲畜人群包虫病的风险因素。方法 用问卷调查的方式收集有关包虫病风险因素的数据。以家庭饲养家畜的人群作为分析细粒棘球蚴病和泡球蚴病风险因素的研究对象。结果 本调查揭示了犬是这些地区泡球蚴病的最重要传染源。19 岁以下的人群大多患细粒棘球蚴病而非泡球蚴病,19~38 岁的人群,尤其是妇女,增加感染泡球蚴病的风险(女对男 OR=2.438,CI=1.317~4.514,P<0.05)。游牧、年龄大、耍犬及食物不防蝇等可增加患细粒棘球蚴病和泡球蚴病的机会。此外,饲养牦牛或绵羊的人群患两型包虫病的风险均增大,饮用不安全水源致使患泡球蚴病的可能性增加。结论 除年龄、性别、环境状况及卫生行为外,饲养牦牛或羊和耍犬也增加了患包虫病的风险。

【关键词】 包虫病;风险因素;调查

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Hydatidosis (HD) is a major public health problem in western Sichuan Province, China. Two types of hydatidosis, i.e. cystic echinococcosis (CE) and alveolar echinococcosis (AE) are known to be endemic in the area. The hydatidosis prevalence rate was 4.0% (161/3 998) in human, the rate of CE was 2.1% (85/3 998) and the rate of AE was 1.9% (77/3 998) according to the investigation from June 1997 to August 1998 in the area[1]. It was reported that the dogs were sources of human infection of *Echinococcus granulosus* and the foxes and some domestic carnivores were sources of human infection of *Echinococcus multilocularis*.[2-4] However, the host and environmental factors that related to hydatidosis are far from clear in the area. In this study, households raising livestock were selected to identify the factors for development of two types of hydatidosis.

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MATERIALS AND METHODS

The cross-sectional investigation was conducted in Ganzi and Shiqu counties, western Sichuan Province. Six sites were selected as investigation sites, which included 4 livestock raising townships, 2 agricultural townships, and 2 urban areas. The same sample collection procedures were used at all sites.

1 Study site

Garze County and Serxu County are under the jurisdiction of Garze Zang Autonomous Prefecture, Sichuan. Garze County borders on Serxu County. The two counties are located at 97°20″ – 100°25″EL and 36°19″ – 31°24″NL. They border on Qinghai in the west. Both counties belong to Qing-Zang Plateau.

2 Data collection

A standard questionnaire was used to interview individuls to collect information on socioeconomic factors, environmental sanitation, the way of residence, the presence of dogs in family, stray dogs and livestock, and related health behaviors. In addition, chest radiography and abdominal B-ultrasonic scanning were used. Blood was drawn for serodiagnosis using the echinococcal dot-ELISA[5] and the *Echinococcus multilocularis*-specific Em18-blotting[6].

3 Statistical procedure

The risk analysis was based on the comparison of patients with non-patients. The statistical procedures were conducted in two phases. In the first phase, prevalence rates and odds ratios for CE and AE associated with a number of factors were calculated. For calculating the odds ratios, the risk factors were put into multinomial logistic regression model separately. The dependent variable had three responses: CE patients, AE patients and non-hydatidosis. The risk factors were age, sex, the way of residing, livestock species raised, keeping dogs, stray dogs found around the house, dogs kept by neighborhood, keeping fox skin products, drinking water source, washing hands before eating, preventing food from flies, and playing with dogs. In the second phase, a multinomial logistic regression model was used to determine the relative effect of each independent variable including those not being found significant in the first phase. All odds ratios were calculated using maximum likelihood estimation, chi-square statistics, and test-based 95% confidence intervals (CIs).

RESULTS

The study population comprised of households raising livestock. A total of 1 858 people were enrolled in the study, representing 46.5% of 3 998 people investigated. Among them, 1 803 people were Zang nationality (Tibetan), constituting 97.0% of the study population.

1 Analysis of single factor

The risk factors (Table 1) whose odds ratios were found statistically significant for CE were: age, the way of residence, the species of livestock raised, protecting food from flies, and playing with dogs occasionally vs. never.

The risk factors whose odds ratios were found statistically significant for AE were: age, sex, the way of residence, drinking water source, protecting food from flies and playing with dogs.

The prevalence rates of CE were higher than those of AE in all age groups. However, only in population below 19 years old, the CE prevalence rate (1.7%) was statistically higher than that of AE (0.2%) (P = 0.00612, Fisher exact test). Younger people had a lower prevalence compared with elder people for both CE and AE. There was a big increase in AE prevalence rate for people aged between 19 and 38 compared with those aged less than 19. No significant defference was found between prevalence rates of population aged between 19 and 38 and population aged more than 38. Although CE and AE prevalence rates of females in both lower age groups were higher than those of male, only female aged between 19 and 38 had a significantly higher AE prevalence rate compared with that of male aged between 19 and 38. The mean age of the female patients in 19 – 38 year-old population was 31.69 (s = 4.84, range = 24 – 38) and the mean age of the patients in 19 – 38 year-old population was 31.89 (s = 34.43, range = 24 – 38).

2 Multiple factor analysis

Table 2 shows the factors found significant by the multiple factor analysis using the multinomial logistic regression model. In this analysis, all variables including those not found significant in single factor analysis were put into the model. Three factors including age, species of livestock raised and playing with dogs were found statistically associated with CE or AE in this model. Other risk factors found significant in the single factor analysis were not found significant in this analysis. However, the factor "species of livestock raised" not found significant for AE in the single factor analysis was significant in this multiple factor analysis.

Table 1　Prevalence rates and odds ratios of selected factors for CE and AE among 1858 people raising livestock in western Sichuan Province, China (June 1997 – August 1998)

Study factor	Prevalence rate of CE	Odds ratio(CI)*	Prevalence rate of AE	Odds ratio(CI)*
Age 1				
Age<=19	1.7%(11/631)	0.289(0.145-0.576)+	0.2%(1/631)	0.037(0.005-0.276)+
19<age<=38	3.2%(20/616)	0.563(0.320-0.990)+	2.9%(18/616)	0.718(0.385-1.337)
Age>38	5.6%(34/611)		3.9%(24/611)	
Age 2				
Age<=19	1.7%(11/631)	0.514((0.244-1.081)	0.2%(1/631)	0.052(0.007-0.390)+
19<age<=38	3.2%(20/616)		2.9%(18/616)	
Sex 1				
Female	3.7%(35/953)	1.122(0.683-1.844)	1.9%(17/953)	1.471(0.793-2.731)
Male	3.2%(30/905)		2.7%(26/905)	
Sex 2				
Female(age<=19)	1.8%(6/330)	1.100(0.332-3.641)	0.3%(1/330)	1.833(0.061-54.832)
Male(age<=19)	1.7%(5/301)		0(0/301)	
Female(19<age<=38)	4.0%(12/297)	1.687(0.680-4.190)	4.4%(13/297)	2.925(1.029-8.311)+
Male(19<age<=38)	2.5%(8/319)		1.6%(5/319)	
Female(age>38)	5.2%(17/326)	0.862(0.431-1.723)	3.7%(12/326)	0.862(0.381-1.952)
Male(age>38)	6.0%(17/285)		4.2%(12/285)	
Nomadic or not				
Non-nomadic	2.8%(40/1351)		1.8%(25/1351)	
Nomadic	5.7%(25/399)	2.116(1.268-3.531)+	4.1%(18/399)	2.438(1.317-4.514)+
Species of livestock				
Sheep or yaks	5.6%(50/894)	3.788(6.803-2.110)+	2.8%(25/894)	1.580(0.855-2.915)
Other livestock	1.6%(15/964)		1.9%(18/964)	
Keeping dogs				
No	3.4%(10/298)		1.7%(5/298)	
Yes	3.5%(55/1560)	1.061(0.534-2.106)	2.4%(38/1560)	1.466(0.572-3.757)
Stray dogs found around residence				
No	3.5%(51/1473)	0.947(0.518-1.730)	2.2%(33/1473)	0.858(0.419-1.757)
Yes	3.6%(14/385)		2.6%(10/385)	
Dogs kept by neighborhood				
No	2.7%(3/110)		0.9%(1/110)	
Yes	3.5%(62/1748)	1.333(0.411-4.316)	2.4%(42/1748)	2.708(0.369-19.867)
Keeping fox skin products				
No	3.1%(25/807)		2.6%(21/807)	
Yes	3.8%(40/1051)	1.231(0.740-2.047)	2.1%(22/1051)	0.806(0.440-1.477)
Drinking water source				
Well or tap water	3.0%(20/675)		1.3%(9/675)	
Ditch, river, or pond	3.8%(45/1183)	1.317(0.771-2.249)	2.9%(34/1183)	2.211(1.054-4.638)+
Washing hands before eating				
Yes	2.8%(27/975)		1.7%(17/975)	
No	4.3%(38/883)	1.600(0.968-2.643)	2.9%(26/883)	1.739(0.937-3.227)
Protecting food from flies				
Yes	2.0%(14/709)		0.8%(6/709)	
No	4.4%(51/1149)	2.366(1.299-4.307)+	3.2%(37/1149)	4.005(1.681-9.539)+
Playing with dogs				
Always	5.3%(25/470)	3.603(1.755-7.399)+	3.8%(18/470)	4.077(1.689-9.843)+
Occasionally	4.2%(29/693)	2.763(1.369-5.577)+	2.6%(18/693)	2.695(1.118-6.495)+
Never	1.6%(11/695)		1.0%(7/695)	

* CI = Confidence interval,　+ Statistically significant

Table 2 Multiple factors analysis of risk factors for CE and AE among people raising livestock in western Sichuan Province, China (June 1997 – August 1998)

Risk factors	Odds ratio (95% CI) of CE	P	Odds ratio (95% CI) of AE	P
Age				
Age<=19 vs. age>38	0.263(0.127–0.547)	0	0.037(0.005–0.282)	0.001
19<Age<=38 vs. age>38	0.593(0.331–1.063)	0.079	0.747(0.396–1.410)	0.368
Raising sheep or yaks vs. raising other livestock	4.827(2.589–9.002)	0	2.217(1.132–4.341)	0.020
Playing with dogs				
Always vs. never	2.004(0.872–4.604)	0.102	2.182(0.814–5.849)	0.121
Occasionally vs. never	2.573(1.234–5.364)	0.012	2.562(1.040–6.314)	0.041

DISCUSSION

This study assessed the impact of a number of common-shared and the different risk factors of AE and CE in areas endemic for both AE and CE in western Sichuan Province. The factors involve demography, socioculture, environment, the mode of living and production, and related behaviors.

The nomadic life style and the species of livestock raised directly influenced the prevalence rate of hydatidosis. In the research area, people having a nomadic life or raising yaks or sheep frequently exposed to the contaminated nature. They certainly had more opportunity to suffer from CE. In the multiple factor analysis, it was found that "raising yak or sheep" increased the probability of suffering from AE. There might be two reasons for that: one was that people raising yaks or sheep actually lived in the grassland with large number of owned dogs, stray dogs and foxes; another one was that the yaks or sheep might play a role in the transmission of AE. However, there was no evidence supporting the second reason so far[7].

Among 18 AE patients in 19 – 38 years old population, 13 AE patients were females. In western Sichuan Province, in the family of herdsmen, the females were responsible for feeding dogs, collecting yaks' dung, taking water, and depasturing the livestock. Compared with the males, the females had more opportunities to be infected with *E. granulosus* and *E. multilocularis* compared with the male.

The fox was thought to be an important transmission source of AE. But the dogs infected with *E. multilocularis* may represent a special infection risk because of their close association to humans[8]. Our analyses found that among the 1 051 people owning fox skin products, only 22 person had fox skin products from the foxes hunted by themselves. However, none of the 22 people suffered from AE or CE. The analyses also did not find the factor of "keeping fox skin products" statistically significant. This confirmed that the fox was a much minor problem compared with the dog. Another potential transmission source of AE is cat. But few cats were kept by local herdsman there.

Both kinds of analyses revealed that keeping dogs and having stray dogs around residence did not directly affect the prevalence rates of CE and AE. It appeared that in areas with large number of dogs, "playing with dogs" was a more direct danger than the factors of "keeping dogs" and "stray dogs found around residence". This behavior was found to be statistically significant associated with both CE and AE. In the multiple analysis, only "occasionally playing with dogs versus never" had a statistically significant odds ratio for both CE and AE.

We conclude from our study that controlling of the dogs, including owned dogs and stray dogs, should be the most important part of any hydatidosis control programme in western Sichuan.

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A canine purgation study and risk factor analysis for echinococcosis in a high endemic region of the Tibetan plateau

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Abstract

The Tibetan plateau of western China has been shown to have a very high prevalence of human cystic echinococcosis (CE) caused by *Echinococcus granulosus* and human alveolar echinococcosis (AE) caused by *Echinococcus multilocularis*. The domestic dog is suspected to be the primary definitive host for the transmission of both *E. granulosus* and *E. multilocularis* to humans in this locality. A purgation study of 371 dogs in Shiqu County, Sichuan Province during 2002–2003 resulted in an *E. multilocularis* prevalence of 12% and an *E. granulosus* prevalence of 8%. These crude prevalences were then adjusted, based on the known sensitivity of arecoline purgation for the detection of *E. granulosus* and a suggested sensitivity for the detection of *E. multilocularis*. In addition, it was assumed that some immature parasites of either species could be misidentified morphologically and wrongly assigned. This resulted in credible true prevalence intervals of between 13–33% for *E. multilocularis* and 8–19% for *E. granulosus*. Prevalences of other intestinal helminthes found on purgation were: *Taenia* spp. 31%, *Dipylidium caninum* 1%, and ascarids 8%. Risk factors associated with the acquisition of canine echinococcosis were evaluated based on responses to a questionnaire administered to dog owners. Male dogs were more likely to be infected with *Echinococcus* spp. than female dogs ($P < 0.05$) and dogs allowed to roam were more likely to be infected with *E. multilocularis* ($P < 0.05$).

Keywords: *Echinococcus*; Epidemiology; Risk factors; Arecoline hydrobromide; China; Prevalence

1. Introduction

Echinococcus granulosus and *Echinococcus multilocularis* are the cestode species responsible for human cystic echinococcosis (CE) and human alveolar echinococcosis (AE), respectively. Shiqu County in Sichuan Province, People's Republic of

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China has been found to harbor one of the highest prevalences of CE and AE ever recorded (Budke et al., 2004). It is speculated that domestic dog is the primary definitive host for both *E. granulosus* and *E. multilocularis* transmission to humans in this region (Wang et al., 2001). The inhabitants of Shiqu County are primarily herdsmen of the Tibetan ethnic group. Due to their physical environment, socio-economic situation, and religious beliefs they live in conditions with a poor standard of hygiene and have a close relationship with their livestock (yak, sheep, and goats) and dogs. Deworming of dogs is not widely performed due to a lack of knowledge of canine intestinal parasites as well as an inability and/or unwillingness to pay for anthelmintics. Herdsmen, in this locality, usually have traditional areas, based on village membership, where they maintain yaks in the summer and the winter. In the winter, often at a time prescribed by the local government, livestock are taken to lower altitude winter pastureland where people normally live in fixed settlements consisting of mud-brick houses. During the spring, yaks are taken to summer pastureland where there are no permanent settlements. Owned dogs, in this region, are valued based on their aggressiveness and kept primarily to guard personal property and livestock. Women are responsible for the feeding and general care of the dog unless there are no females in the household. Feeding of raw offal to dogs is a rule rather than an exception as is permitting stray dogs to roam in the vicinity. Strong Buddhist beliefs do not allow for the elimination of stray dogs and many strays are actually fed and "adopted" by households or monasteries. Since there are very few abattoir facilities in the area, most slaughtering and carcass disposal is performed at home. Screening, via abdominal ultrasound, for the identification of human echinococcosis has been carried out previously in western Sichuan Province (Wang et al., 2001; Budke et al., 2004). However, no extensive studies of infection in the owned dog definitive host have been previously conducted.

2. Materials and methods

2.1. Arecoline hydrobromide purgation

During the Spring of 2002 and the Spring and Autumn of 2003, the parasympathomimetic purgative agent arecoline hydrobromide (Boehringer Ingelheim) was used to collect intestinal parasites from 371 owned dogs in Shiqu County. Dogs were administered 7 mg/kg arecoline hydrobromide in a food-ball after obtaining owner consent and explaining potential side effects of treatment. Purged material was collected in leak-proof bags and saturated in either 10% formal saline or 85% ethanol until examination of the material could be conducted. After purgation, the site was buried and dog owners were instructed to interact with their dog using caution due to the potential presence of zoonotic parasites. Purged samples were taken to the Sichuan Institute of Parasitic Diseases (SIPD) in Chengdu, Sichuan Province, PR China where helminthes were removed, counted, and placed in 10% formal saline or 85% ethanol depending on the preservative agent originally used for the sample. Parasitic material was later transported to the Institute of Parasitology, University of Zürich for further speciation based on microscopic examination.

2.2. Analysis

All data was entered into an Excel spreadsheet (Microsoft, Redmond, WA) where prevalence and abundance were calculated. Exact 95% binomial confidence intervals were assigned to prevalence calculations and 95% negative binomial confidence intervals were assigned to abundance data utilizing the likelihood profile tool of the Excel add-on PopTools (CSIRO, Australia) (Torgerson et al., 2003a). True prevalence estimates of *E. granulosus* and *E. multilocularis* were determined based on the suggested sensitivity and specificity of arecoline hydrobromide purgation.

Specificity of purgation has been reported to be 100%. This is likely to be true at the genus level, but since both *E. granulosus* and *E. multilocularis* are present in the region, it was assumed that some misidentification could take place especially in regards to immature worms. Therefore, the specificity of *E. granulosus* detection on purgation was based on the portion of the *E. granulosus* lifespan spent in the immature stage (approximately 15%) (Thompson, 1995). The assumption was made that about one half of the immature worms would be misidentified resulting in a specificity of approximately 92%.

Specificity of purgation of *E. multilocularis* was determined in a similar manner to *E. granulosus*, with 17% of the adult worm lifespan in the immature stage (Eckert, 1998). Assuming that one half of the immature worms would be misidentified, this leads to a specificity of approximately 92%. Crude prevalences of *E. granulosus* and *E. multilocularis* were then modeled as binomial distributions, with each value in the distributions having a 92% chance of being correct and an 8% chance of being misidentified. Since the only real possibility for misidentification of *E. granulosus* or *E. multilocularis* is with the other species, lost specificity for the diagnosis of one worm was allocated to the other species and vice versa. The random variable generator function of PopTools was utilized to produce the data sets which were then resampled 10,000 times using the same program.

Schantz (1997) reported that of 46 true *E. granulosus* positive dogs identified on postmortem examination, 30 animals produced a positive purge following a single treatment with arecoline. This was used as the basis of a beta distribution to model the true sensitivity of arecoline purgation of *E. granulosus*, with parameters 31 and 17. The random variable generator function of PopTools was used to produce the distribution, which was then resampled 10,000 times. Each iteration was used to calculate the true prevalence based on the observed prevalence and the specificity. Based on results of the only known published study where *E. multilocularis* was found on purgation of dogs, a distribution was assigned to the sensitivity of *E. multilocularis* purgation (Stefanic et al., 2004). In this study, 131 dogs were purged with 4 positively identified as *E. multilocularis* on purgation. In addition, PCR was able to identify a further two *E. multilocularis* positive dogs resulting in an estimated sensitivity of 67%. A total of six dogs found to be *Echinococcus* spp. purge positive were not picked up on PCR analysis. The species of these worms where, however, not reported. In order to set the lower and upper limits of the sensitivity distribution, minimum and maximum true positive and purge positive estimates were determined. This resulted in a minimum of 6 and a maximum of 12 true positive cases and a minimum of 4 and a maximum of 10 purge positive cases, with the assumption being made that there were no true positive cases that were negative on both PCR and purgation. Based on these finding, a minimum of 33% (4/12) and a maximum of 83% (10/12) was used for specificity calculations. A triangular distribution was then assigned to the specificity of *E. multilocularis* purgation with an average of 67%, a minimum of 33%, and a maximum of 83%. A triangular distribution is a continuous distribution that is typically used to describe an outcome based on knowledge of the minimum and maximum values and an inspired guess of what the modal value may be. The random number generator function of PopTools was employed to produce the distribution, which was then resampled 10,000 times and each iteration used to calculate a true prevalence.

The 10,000 new observed prevalence data sets, based on an approximate 92% specificity for arecoline purgation, were then divided by the 10,000 data sets for sensitivity and the upper and lower 2.5 percentiles calculated to arrive at 95% credible true prevalence intervals for *E. granulosus* and *E. multilocularis*. No data is available that would indicate the sensitivity of arecoline purgation for the other helminthes detected, therefore, no adjustments were made to their purgation based prevalences. In order to investigate if there was any association between the burdens of different parasite species, and hence evidence for similar transmission mechanisms, $\log(n+1)$ transformed burdens of each parasite were correlated against the burdens of each other species or group detected to construct a correlation matrix.

2.3. Risk factor questionnaire

A twenty-eight question survey, written in both English and Mandarin Chinese, was administered orally to dog owners willing to participate in the purgation study. One questionnaire was filled out for each dog being tested. The first set of questions included general information about the dog owner such as name, village name, and occupation. The next set focused on the dog being tested and included age, gender, name, and a brief physical description. Questions about the feeding habits of the dog, human interaction with the dog, history of fox hunting, and whether or not there were stray dogs in the area were asked. Information on livestock ownership, water source, and any previously diagnosed cases of human echinococcosis in the household was also obtained. The questionnaire concluded with questions that

Table 1
Purgation results for dogs ($n = 371$) in Shiqu County, Sichuan Province, PR China (2002–2003)

Parasite	Prevalence (%)	Confidence limits or credibility interval	Mean abundance	Confidence limits[a]
E. granulosus				
Crude	8.35	5.75–11.65[b]	80	32.60–288.96
Adjusted	12.7	8.3–18.8[c]		
E. multilocularis				
Crude	12.13	8.99–15.89[b]	131	61.58–362.44
Adjusted	19.7	13.4–32.7[c]		
Taenia spp.	31.00	26.32–35.98[b]	1.32	1.016–1.7506
D. caninum	1.08	0.29–2.74[b]	0.0189	0.00517–0.10485
Ascarids	7.55	5.07–10.72[b]	0.124	0.0794–0.19636

Crude prevalence represents actual prevalence found upon arecoline purgation, while adjusted prevalence represents prevalence after purgation sensitivity and specificity have been taken into account.

[a] Negative binomial 95% confidence limits.

[b] Exact binomial 95% confidence limits.

[c] Credibility interval based on assumptions on the sensitivity and specificity of arecoline purgation.

evaluated the participant's knowledge of echinococcosis and its acquisition. Questions were designed so that the majority of responses could either be circled or answered in only a few words in order to minimize any misunderstandings during translation. All questionnaires were identified by the date, a unique numerical identifier, and GPS coordinates. After the questionnaire was completed, information regarding the *Echinococcus* spp. life cycles and mode of transmission to humans was provided to the participant.

Dogs were identified as being infected with *Echinococcus* if adult *Echinococcus* spp. were found upon purgation. Information obtained from the questionnaire was inputted into an Epi Info 2000 version 3 database (CDC, Atlanta, GA) and univariate and multivariate logistic regression performed utilizing the same program. A total of 371 questionnaires were evaluated for risk factors associated with echinococcosis in owned dogs. All dogs infected with *Echinococcus* spp. were first evaluated together. Dogs diagnosed with *E. granulosus* infection were then separated from those diagnosed with *E. multilocularis*, with dogs having a dual infection evaluated in both analyses.

3. Results

Purgation of 371 dogs in Shiqu County during 2002–2003 resulted in an overall *E. multilocularis* prevalence of 12% and an overall *E. granulosus* prevalence of 8% (Table 1). Credible true prevalence intervals were calculated to be 13–33% for *E. multilocularis* and 8–19% for *E. granulosus*. The prevalences of other intestinal helminthes found on purgation were: *Taenia* spp. 31%, *Dipylidium caninum* 1%, and ascarids 8% (Table 1). Mean abundance (the mean number of parasites per host) of *E. granulosus* was 80 worms and mean abundance of *E. multilocularis* was 131 worms (Table 1). Mean intensity of infection (the mean number of parasites per infected host) with *E. granulosus* was 959 worms, with a mean intensity of 1084 worms for *E. multilocularis* infection. A correlation matrix of parasite burdens of the various species or group found on purgation indicated weak yet significant correlations between *E. multilocularis* and *Taenia* spp., *E. multilocularis* and *D. caninum*, *E. granulosus* and *Taenia* spp., *Taenia* spp. and *D. caninum*, and *Taenia* spp. and ascarids (Table 2).

Questionnaires ($n = 371$) were evaluated for risk factors associated with the acquisition of *Echinococcus* spp. infection in dogs. Univariate analysis demonstrated that a dog being male ($P < 0.05$) was a significant risk factor for canine *Echinococcus* spp. infection (Table 3). Having a dog over 3 years of age (mean age of tested dogs = 4.1 years), not keeping a dog tied all of the time, yak ownership, sheep, and/or goat ownership, and having a dog who is known to eat small mammals were not found to be significant risk

Table 2
Correlation matrix for log-transformed parasite abundance

	E. multilocularis	*E. granulosus*	*Taenia* spp.	*D. caninum*	*Ascarids*
E. multilocularis		−0.034	**0.166**	**0.114**	0.049
E. granulosus	−0.034		**0.240**	−0.025	0.026
Taeniia spp.	**0.166**	**0.240**		**0.137**	**0.177**
D. caninum	**0.114**	−0.025	**0.137**		0.021
Ascarids	0.049	0.026	**0.177**	0.021	

Correlation coefficients in bold are considered significant at the 95% confidence level.

Table 3
Univariate analysis for possible variables associated with the acquisition of canine *Echinococcus* spp. infection ($n = 371$)

Variable	Odds ratio	95% Confidence interval	*P*-value
Dog is tied all of the time (dichotomous)	0.6730	0.3753–1.2069	0.1838
Household has yaks (dichotomous)	1.7840	0.6726–4.7320	0.2448
Household has sheep/goats (dichotomous)	1.5182	0.8910–2.5868	0.1247
Dog has been seen eating small mammals (dichotomous)	0.9662	0.5797–1.6103	0.8950
Dog is >3 years of age (dichotomous)	0.8557	0.5135–1.4260	0.5499
Dog is male (dichotomous)	2.5252	1.1041–5.7754	0.0282

factors for *Echinococcus* spp. infection in owned dogs ($P > 0.05$). Multivariate logistic regression also indicated that a dog being male was a significant risk factor for infection with *Echinococcus* spp. ($P < 0.05$) (Table 4). Univariate analysis indicated that not having a dog tied all of the time versus keeping a dog tied all of the time was a significant risk factor for *E. multilocularis* infection ($P < 0.05$) (Table 5), with multivariate analysis confirming the finding (Table 6). The same factors were evaluated for *E. granulosus* infection in dogs, with none found to be significant risks for infection on univariate or multivariate logistic regression analysis (data not shown).

4. Discussion

E. granulosus and *E. multilocularis* purgation based prevalences in owned dogs from Shiqu County are grounds for concern in regards to transmission to humans, especially in light of the high AE and CE levels reported in abdominal ultrasound screened humans from the same county (Budke et al., 2004). In addition, intestinal parasite prevalence based on purgation is most likely an underestimate of true prevalence. Distributions were, therefore, utilized to encompass what is known about the sensitivity and specificity of purgation based on data currently available, with both the prevalences found on purgation and the prevalences adjusted for the sensitivity and specificity of arecoline purgation reported here. Sensitivity of arecoline hydrobromide purgation of *E. granulosus* was found to be 65% after a single dose of arecoline in a study where 118 dogs were purged and subsequently euthanized and necropsied (Schantz, 1997). In regards to *E. multilocularis*, one previous study reported detecting *E. multilocularis* using arecoline to purge dogs, however, information on

Table 4
Multivariate analysis of possible risk factors for acquisition of canine *Echinococcus* spp. infection ($n = 371$)

Variable	Odds ratio (95% CI)	Regression coefficient	S.E.	*P*-value
Dog is tied all of the time (dichotomous)	0.6755 (0.3743–1.2190)	−0.3924	0.3012	0.1928
Household has yaks (dichotomous)	1.4700 (0.5393–4.0069)	0.3852	0.5116	0.4515
Household has sheep/goats (dichotomous)	1.3692 (0.7906–2.3711)	0.3142	0.2802	0.2622
Dog is male (dichotomous)	2.4554 (1.0684–5.6431)	0.8983	0.4246	0.0344

Variables with $P < 0.25$ on univariate analysis were included in multivariate analysis.

Table 5
Univariate analysis for possible variables associated with the acquisition of canine *E. multilocularis* infection ($n = 371$)

Variable	Odds ratio	95% Confidence interval	*P*-value
Dog is tied all of the time (dichotomous)	0.3770	0.1630–0.8721	0.0226
Household has yaks (dichotomous)	1.2328	0.4166–3.6480	0.7053
Household has sheep/goats (dichotomous)	1.4546	0.7609–2.7807	0.2570
Dog has been seen eating small mammals (dichotomous)	1.2267	0.6574–2.2889	0.5209
Dog is >3 years of age (dichotomous)	1.0981	0.5886–2.0484	0.7687
Dog is male (dichotomous)	1.9542	0.7415–5.1500	0.1754

Table 6
Multivariate analysis of possible risk factors for acquisition of canine *E. multilocularis* infection ($n = 371$)

Variable	Odds ratio (95% CI)	Regression coefficient	S.E.	*P*-value
Dog is tied all of the time (dichotomous)	0.3693 (0.1593–0.8558)	−0.9962	0.4288	0.0202
Dog is male (dichotomous)	2.0350 (0.7683–5.3903)	0.7105	0.4970	0.1528

Variables with $P < 0.25$ on univariate analysis were included in multivariate analysis.

sensitivity of purgation for detecting *E. multilocularis* is lacking (Stefanic et al., 2004). Sensitivity estimates for *E. multilocularis* purgation are based on purge results in comparison to PCR findings which, in contrast to necropsy, is not considered a gold standard test. Therefore, a triangular distribution was utilized to model this uncertainty. Specificity was also adjusted for the Shiqu County study based on the premise that since both *E. granulosus* and *E. multilocularis* are present at the study site, some degree of misidentification could occur, especially in regards to immature worms.

Although all associations between parasite burdens identified in this study are weak, the strongest was found between *E. granulosus* and *Taenia* spp. This makes sense in regards to the common mode of transmission between *E. granulosus* and those *Taenia* spp. that utilize a livestock intermediate host. These findings may indicate that the same livestock are commonly infected with both *E. granulosus* and *Taenia* spp. or that certain dogs have more access to infected livestock and thus tend to acquire parasites transmitted from these animals. Further speciation will, however, enable differentiation of taeniids that use small mammal intermediate hosts from those that use livestock. Other weak, yet significant, correlations were found between *Taenia* spp. and all other parasites evaluated and between *D. caninum* and *E. multilocularis*. *Taenia* spp. association with *E. multilocularis* can be due to common intermediate hosts of *E. multilocularis* and some *Taenia* spp. The association between *Taenia* spp. and ascarids can also be attributed, to some extent, to similar means of transmission (from intermediate or paratenic hosts, respectively). Correlations between *D. caninum* and both *Taenia* spp. and *E. multilocularis* must be addressed with the most skepticism since *D. caninum* was found in very few tested dogs and the mode of transmission is different for *D. caninum* compared to the other parasites evaluated. One possible explanation is higher susceptibility in certain hosts to multiple parasitism, but in this study there is very little evidence to support this theory.

The significant risk factor, for owned dog *Echinococcus* spp. infection, of a dog being male may indicate that male dogs are more likely to maintain territory and hunt compared to female dogs. This can be compared to the situation of foxes in Switzerland where male foxes and especially sub-adult male foxes have been shown to carry the majority of the *E. multilocularis* biomass and are known to travel further than their age-matched female counterparts (Hofer et al., 2000). A higher risk in male dogs does not appear to be associated with male dogs being tied less than female dogs, with no significant difference found between the prevalence of tied male versus that of tied female dogs ($P > 0.05$). A dog being male does appear to have a non-significant impact for both *E. granulosus* and *E. multilocularis*, however, when evaluated independently their *P*-values were both greater than the statistically significant cut-off point 0.05 being used here. The significant risk factor, for *E. multilocularis* infection in owned dogs, of not having the dog tied all of the time indicates that these dogs have an increased opportunity to hunt and, therefore, have more access to infected small mammal intermediate hosts. Risk factor analysis for human CE and AE is not a new method and has been performed in multiple countries and regions (Carmona et al., 1998; Dowling and Torgerson, 2000; Dowling et al., 2000; Craig et al., 2000; Yamamoto et al., 2001; Torgerson et al., 2003b). Risk factors associated with canine echinococcosis have not, however, been previously evaluated. Looking at potential factors associated with the acquisition of *Echinococcus* spp. by the definitive host allows for a more current picture of the situation versus evaluation of human cases, which may have been acquired up to ten years prior to the survey.

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Epidemiology of alveolar echinococcosis with particular reference to China and Europe

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SUMMARY

Human alveolar echinococcosis (AE), caused by the metacestode of the fox tapeworm *Echinococcus multilocularis*, is the most pathogenic zoonosis in temperate and arctic regions of the northern hemisphere. Prospective collection of human cases in some areas and mass screenings using ultrasound imaging and confirmation with serological techniques have markedly improved our knowledge of the epidemiology of the disease in humans during the past two decades. Transmission occurs when eggs of the tapeworm, excreted by the final hosts (usually foxes but also dogs, wolves and cats), are ingested accidentally by humans or during normal feeding by a variety of rodents and small lagomorphs. However, the species of host animals differ according to regional changes in mammalian fauna. This review mostly focuses on epidemiology of alveolar echinococcosis in those parts of the world where new and more accurate epidemiological data are now available, i.e. China and Europe, as well as on new epidemiological trends that can be suspected from recent case reports and/or from recent changes in animal epidemiology of *E. multilocularis* infection. The People's Republic of China (PRC) is a newly recognized focus on AE in Asia. Human AE cases were firstly recognized in Xinjiang Uygur Autonomous Region and Qinghai Provinces at the end of 1950s and infected animals were first reported from Ningxia in central China and north-east of Inner Mongolia in the 1980s. *E. multilocularis* (and human cases of AE) appears to occur in three areas: (1) Northeastern China (northeast focus): including Inner Mongolia Autonomous region and Heliongjiang Province (2) Central China (central focus): including Gansu Province, Ningxia Hui Autonomous Region, Sichuan Province, Qinghai Province and Tibet Autonomous Region and (3) Northwestern China: including Xinjiang Uygur Autonomous Region, bordered with Mongolia, Russia, Kazakhstan and Kyrgyzstan. The highest prevalence of the disease, up to 15 per cent of the population in some villages, is reached in China. In Europe, data from the European Echinococcosis Registry (EurEchinoReg: 1982–2000) show 53 autochthonous cases of AE in Austria, 3 in Belgium, 235 in France, 126 in Germany, 1 in Greece, and 112 in Switzerland, and 15 'imported' cases, especially from central Asia; 14 cases were collected in Poland, a country not previously considered endemic for AE. Improved diagnostic technology, as well as a real increase in the infection rate and an extension to new areas, can explain that more than 500 cases have been reported for these 2 decades while less than 900 cases were published for the previous 7 decades. New epidemiological trends are related to an unprecedented increase in the fox population in Europe, to the unexpected development of urban foxes in Japan and in Europe, and to changes in the environmental situation in many countries worldwide due to climatic or anthropic factors which might influence the host–predator relationship in the animal reservoir and/or the behavioural characteristics of the populations in the endemic areas.

Key words: Alveolar echinococcosis, *Echinococcus multilocularis*, epidemiology, animal hosts, risk factors, geography.

INTRODUCTION

Human alveolar echinococcosis (AE), caused by the metacestode of the fox tapeworm *Echinococcus multilocularis*, is considered to be the most pathogenic zoonosis in temperate and arctic regions of the northern hemisphere. In fact no cases have ever been observed in the southern hemisphere, and the lowest latitude for endemic areas is about 28°N in Asian territories. AE cases in humans have been reported from three continents: North America, Europe and Asia. Three human cases reported from Tunisia may indicate that the disease is also present in North-Africa (Robbana *et al*. 1981); however, no confirmation of the species of *Echinococcus* involved in these cases, in that country where *E. granulosus* infection is highly prevalent, has ever been given, and no new cases have been reported since 1981. Fig. 1 summarises the geographic distribution of *E. multilocularis* in the world and the countries which are considered either as endemic areas, or potential ones when only isolated cases have been reported.

The primary target organ for the larva is the liver where it proliferates slowly, but it also spreads into extrahepatic structures and even metastasises to distant organs. Prognosis of AE has improved during

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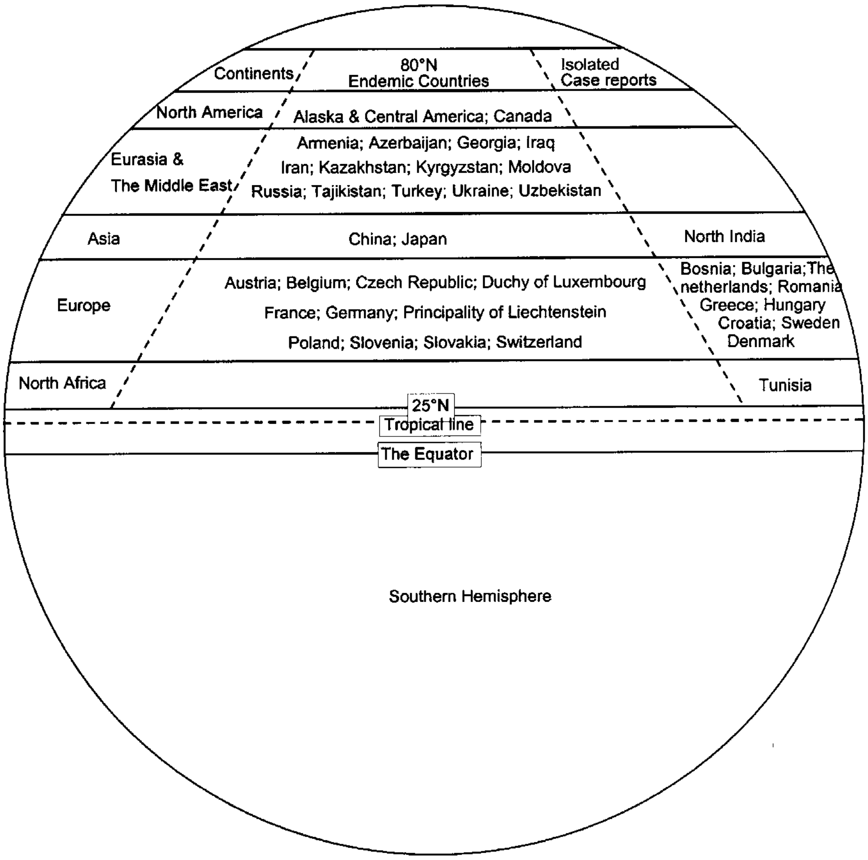

Fig. 1. Schematic representation of alveolar echinococcosis distribution in the world. Neither human cases nor *E. multilocularis* infection in animals have ever been reported in southern hemisphere. For most of the reported isolated cases, confirmation of the diagnosis of echinococcosis and/or of the species of *Echinococcus* involved was not given.

the past 2 decades in those countries where the appropriate and always complex therapeutic strategy may be applied; it remains poor if diagnosed late, and/or when access to medical care is not available or difficult (Vuitton, 1990; Ammann & Eckert, 1995; Bresson-Hadni *et al.* 2000). Diagnosis of the disease, which has a long (5–20 yrs) asymptomatic stage, mainly relies on the availability of good quality imaging techniques, which explains why accurate epidemiological data in many parts of the world have been only available in the past 2 decades. Ultrasound imaging has transformed the diagnostic approach of AE, and has made diagnosis of asymptomatic cases possible in hospital settings, even in remote parts of the world. CT-scan and Magnetic Resonance Imaging are mainly used for confirmation and pre-treatment assessment and staging (Ammann & Eckert, 1995; Bresson-Hadni *et al.* 2000). Especially, mass screenings using ultrasound imaging and confirmation with serological techniques have markedly improved our knowledge of the epidemiology of the disease in humans (see Macpherson, Bartholomot & Frider, in this supplement). Many excellent reviews on epidemiology of AE in Europe have been published (Stössel, 1989; Fessler, 1990; Eckert, 1996, 1997; Eckert & Deplazes, 1999; Eckert *et al.* 2000, 2001) and a comprehensive analysis of the data available on the spread of the disease in the world until the beginning of the 1990s can be found in Schantz *et al.* (1995).

Presence of human cases of AE is highly dependent of the presence of an actively functioning parasitic cycle in nature and thus understanding the local aspects of this cycle in a given region is essential to understand human epidemiology (Deplazes & Eckert, 2001). The natural transmission cycle of *E. multilocularis* is universally uniform in pattern, i.e. small mammals (rodents, pikas) act as intermediate hosts and carnivores of various species are definitive hosts. Transmission to humans occurs when eggs of the tapeworm, excreted by the final hosts (usually foxes but also dogs, wolves and cats), are ingested accidentally. However, the species of the host animals differ according to regional changes in mammalian fauna. Throughout the holarctic tundra zone, the cycle is completed through the predator–prey relationship existing between foxes, primarily the arctic fox (*Alopex lagopus*) and rodents of the genera *Microtus*, *Clethrionomys* and *Lemmus*. In central Europe, the cycle involves red foxes (*Vulpes vulpes*) and voles of various species, whereas in North America, the natural cycle involves coyotes (*Canis latrans*) and *V. vulpes* as final hosts. The predator–prey interactions between definitive and intermediate hosts (Rausch,

Table 1. Definitive hosts (carnivores) recorded as susceptible species for *E. multilocularis* infection in the world (according to Zhou, H. X., 2001)

Carnivores	Places
Arctic fox (*Alopex lagopus*)	Former USSR; North America
Red fox (*Vulpes vulpes*)	Asia; Eurasia; The middle East Europe; North America
Corsac fox (*Vulpes corsac*)	China; Former USSR
Tibetan fox (*Vulpes ferrilata*)	China
Dog (*Canis familiaris*)	Alaska; Europe; China; Former USSR
Wolf (*Canis lupus*)	China; Former USSR
Coyote (*Canis latrans*)	North America
Wild cat (*Felis libyca*)	Former USSR
Cat (*Felis catus*)	Europe; Former USSR
Raccoon-dog (*Nyctereutes procyonoides*)	Former USSR
Grey fox (*Urocyon cinereoargenteus*)	Central North America

1995), as well as susceptibility and immunity of hosts (Vuitton, 2003), play a key role in the parasite transmission cycle. This includes seasonal fluctuations in numerical density of the intermediate host and the diversity of diet of the definitive host (see Giraudoux *et al*. 2002, and in this supplement) and fertility of the adult as well as larval stages of the cestode in animal hosts (Vuitton *et al*. 2002; Craig *et al*. in this supplement). Tables 1 and 2 give a list of the definitive and intermediate hosts respectively recorded as susceptible species for *E. multilocularis* in the world.

This review will mostly focus on epidemiology of alveolar echinococcosis in those parts of the world where new and more accurate epidemiological data are now available, i.e. China and Europe, as well as on new epidemiological trends that can be suspected from recent case reports and/or from recent changes in animal epidemiology of *E. multilocularis* infection. The land-mass of PR China is a huge, and detailed epidemiological data mainly obtained from the scientific literature in Chinese and from mass screenings performed in the past decade, have relatively recently become available. In the absence of data published in international journals, published materials of various sources (non-English language, PhD thesis dissertations) have been used whenever necessary, after checking carefully for accuracy and reliability. Whenever available, data on the animal hosts of *E. multilocularis* have been given for every region studied, especially when particularities might explain risk factors in a given area and/or when they were associated with land use or behavioural characteristics useful to understand human epidemiology.

ALVEOLAR ECHINOCOCCOSIS IN NORTH AMERICA

The parasite has been recorded in two distinct geographic regions, the north tundra zone (western Alaska) and central north America (centred on southern Manitoba and North Dakota) (Storandt *et al*. 1993, 2002). Very high prevalence of AE in Eskimo communities in Alaska, especially on St Lawrence Island, in the northern part of the Bering Sea, was observed between 1950 and 1990 (Rausch & Schiller, 1956; Wilson & Rausch, 1980; Stehr-Green *et al*. 1988). A mass survey using specific serology was undertaken in the 1980s and led to the discovery of 'abortive cases' (or 'aborted cases'), i.e. patients with a positive highly specific serology and calcified lesions in the liver that were found sterile when operated on (Rausch *et al*. 1987). This endemic focus does not seem to have progressed, since no reports on a significant number of new cases have been published in the past 10 years. Transmission to humans occurred through arctic foxes, with a prevalence of infection averaging 77% and could be in excess of 90%, that preyed on northern voles, especially *Microtus oeconomus* considered as the main intermediate host for *E. multilocularis*, and a varying lemming (*Dicrostonyx exsul*), the northern red-backed vole (*Clethrionomys rutilus*) and shrews (*Sorex cinereus*) (Rausch, Fay & Williamson, 1990). Village dogs, found infected in 1951 with a prevalence of 12%, were also considered important in the spreading of the parasite close to human communities (Rausch & Fay, 2002) and baiting of these dogs with praziquantel was adopted as a control measure on St Lawrence Island in the 1980s (Rausch, Wilson & Schantz, 1990).

In central North America, despite the presence of infected definitive and intermediate hosts, in North and South Dakota, Iowa, Minnesota, Montana, Wyoming, Nebraska, Illinois, Wisconsin, Indiana, and Ohio, and 3 contiguous Canadian provinces, with prevalences quite similar to those found in highly endemic areas elsewhere in the world, only 2 human cases have been reported; the first, diagnosed in 1957, from Winnipeg, and the second, in 1977, from southeastern Minnesota. Serological screening of 120 fox trappers in South Dakota failed to detect any positive cases (Storandt & Kazacos, 1993; Storandt *et al*. 2002; Schantz *et al*. 1995). Behavioural more than genetic factors may be hypothesised to explain

Table 2. Intermediate hosts (small mammals) recorded as susceptible species for *E. multilocularis* infection in the world (according to Zhou, H. X., 2001)

Family	Species	Location
Soridae (1 genus)	*Sorex jacksoni*	St Lawrence
Talpidae (1 genus)	*Talpa altaica*	Altai Krai
Sciuridae (3 genera)	*Sciurus vulgaris*	Iakutiia
	Citellus ungalatus	St Lawrence; Buriat-Mongolia
	C. alashanicus	Ningxia
	Marmota bobak	Pavlodarsk Oblast'
Cricetidae (6 genera)	*Neotoma cinerea*	Wyoming
	Peromyscus maniculatus	North America
	Cricetus cricetus	Western Siberia
	Meriones unguiculatus	Buriat (Mongolia); Inner Mongolia
	M. erythourus	Kazakhstan
	Meriones spp.	Iran
	Rhombomys opimus	Aktiubinsk-Oblast'; Kazakhstan
	Myospalax myospalax	Kazakhstan
	M. fontanieri	Ningxia
Muridae (3 genera)	*Apodemus agrarius*	Kazakhstan
	A. sylvaticus	Tselinogradsk Oblast'
	Mus musculus	Europe; Xinjiang
	Nesokia indica	Iran
Arvicolidae (7 genera)	*Microtus arvalis*	Germany; France; Switzerland; Russia
	M. oeconomus	Kurile Islands; St Lawrence; West Alaska
	M. socialis	Georgia
	M. roerti	Georgia
	M. irene	Sichuan
	M. hyperboreus	Iakutiia
	M. gregalis	Kazakhstan; Kyrgyzstan
	M. brandti	Inner Mongolia
	M. pennsylvanicus	North America
	Arvicola terrestris	France; Western Siberia
	Ondatra zibethicus	Russia; Kazakhstan; France; Germany; North America
	Lagurus lagurus	Tselinogradsk Oblast'
	Ellobius talpinus	Kyrgyzstan
	Lemmus sibiricus	Eurasia tundra
	Clethrionomys glareolus	Latvia
	C. rufocanus	Iakutiia
	C. rutilus	Hokkaido; Karaginsk; Kamachatka Novosibirsk Oblast'
Dipodidae (1 genus)	*Allactaga elater*	Azerbaizhan
Ochotonidae (1 genus)	*Ochotona daurica*	Tuva
	O. pricei	
	O. roylei	Kyrgyzstan
	O. curzoniae	Sichuan; Qinghai
Leporidae (1 genus)	*Lepus oiostulus*	Sichuan

the apparent discrepancy between the prevalence of animal and human infection in this area.

ALVEOLAR ECHINOCOCCOSIS IN CENTRAL ASIA

Human cases were reported from the former USSR, throughout Russia and most of the newly independent states including Ukraine, Byelorussia, Moldova, Georgia, Armenia, Azerbaijan, Kazakhstan, Uzbekistan, Tajikistan, and Kyrgyzstan (Lukashenko, 1968; Yarotskii *et al.* 1988; Schantz *et al.* 1995). Reviews by Bessonov (1998; 2002) report that some of the highest prevalence rates ever reported before the Chinese focus was studied (i.e. 10/100 000 and more) were recorded in Yakutia, Chukot, and Korjak autonomous districts, Kamchatka, Omsk and Tomsk regions and Altai territory. Medium prevalence rates (1–10/100 000) were recorded in Tuva republic, at the south of Krasnoiarsk territory, Magadan region and northern areas of Kazakhstan. Lower prevalence rates were recorded in some zones of west Siberia, East Povolzhje, Byelorussia, north Caucasus, and Azerbaijan. Most cases in the highly endemic region of Kamchatka were limited to indigenous people with activities in hunting and herding (Yarotskii *et al.* 1988). Unfortunately no update in the epidemiology of AE in Russia is available. Data given in the most recent publications are often old and fragmentary and need to be reviewed; no systematic mass-screening has ever been performed and/or published in Russia and the independent states of central Asia, which certainly represent one of the most endemic areas in the world. In fact nine species of carnivores (arctic fox, red fox, corsac fox, wolf, golden jackal, rural dog, racoon dog, wild cat and domestic cat) have been found naturally infected, as well as 30 species of small mammals, including voles, mice, shrews, lemmings, marmots, jirds, muskrats, ground squirrels, jerboas, hares and hamsters (Bessonov, 1998). It is likely that the parasite cycle is still very active, and that human cases still occur. The situation regarding AE was recently re-assessed in Kazakhstan: an average of 20 new human cases are observed each year in the eastern part of the country; the larval stage was found in 18 species of rodents, including marmots, steppe marmot (*Marmota bobac*) and grey marmot (*Marmota baibacina*), and gerbils, red-tailed gerbil (*Meriones libycus*) and great gerbil (*Rhomomys opimus*), especially in the forest-steppe, steppe zones and river valleys, and the adult stage in 4 species of definitive hosts, foxes (*Vulpes vulpes* and *V. corsac*), domestic dog (*Canis familiaris*), especially hunters' dogs, and wild cat (*Felis lybica*) (Shaikenov & Torgerson, 2002).

Isolated cases have been reported from northwest Iran, northern Iraq, southern Azerbaizhan and Afghanistan (Zarrifar, 1997; Al Irhayim, personal communication), and the natural cycle is known to be present in this area (Rausch, 1995), but most cases in central/western Asia have been diagnosed in Turkey. Cases of non-European origin recorded in the EurEchinoReg registry from 1982 to 2000 were born (and likely contracted infection) in the Newly Independent States (3 cases), Kazakhstan (1 case), Afghanistan (1 case) and in Turkey (3 cases). Among the 157 autochtonous Turkish cases reported from 1934 to 1983, 90% originated from central, eastern Anatolia and the Black sea and only 2% from the European part of Turkey (Uysal & Paksoy, 1986; Stössel, 1989). In a series of 39 surgical cases, more than 90% came from the eastern, Asian, part of Turkey. Between 1980 and 1998, 189 AE cases were collected from different regions. The ages ranged from 7 to 70 years for these 119 cases; 49 (41%) were males and 70 (59%) were females. The origin of most of the patients was from eastern Anatolia (57%), especially from Erzurum (Altintas, 1997). Associated with the EurEchinoReg programme described below, Altintas collected 202 cases from 1980 to 1998 (Kern *et al.* 2003). In all Middle East and central Asian countries where AE cases were reported from, both *Echinococcus* spp. are responsible for human disease and confusion is possible. However, in Turkey, the collection of AE cases originated mostly from surgery, and the cases were confirmed by pathological examination. The role of the various potential definitive and intermediate hosts in transmission to humans is still unknown; presence of *E. multilocularis* in a fox, in the north-west of Turkey, was reported by Merdivenci in 1965 (cited in Altintas, 1997). Research projects are currently considered for both Turkey and Iran.

ALVEOLAR ECHINOCOCCOSIS IN EASTERN ASIA

Japan

The first human case of AE was recognised in 1936 in Hokkaido, the northern island of Japan (Tunoda, Mikami & Aoki, 1937; Suzuki, Sato & Uchino, 1993). *E. multilocularis* was introduced with infected foxes transferred to Rebun Islands, northwest of Hokkaido from the Kuriles islands, to fight against rodents, in years 1924–26. Another transfer of foxes took place in the 1960s. A total of 383 human AE cases were detected since then, up to 1999, and 5–9 cases per year are newly disclosed by the Committee for Echinococcosis Control in Hokkaido (Tsukada *et al.* 2000). Periodic serological screening of potentially exposed populations over the past 25 years has shown that farm residents were the population group the most at risk in Japan, due to faecal contamination by foxes that scavenge in the proximity of farms. The fox is the animal symbol of Hokkaido Island and rather well tolerated by farmers; approaching foxes has become a tourist attraction in some parts of Hokkaido, and this could be a reason of extension of the diseases to the subjects from other islands of Japan (Takahashi, personal communication). In fact, a report of 60 AE cases on Honshu, the main island of Japan, has been published (Kamiya, 1988; see also Ito *et al.* in this supplement); 17 would be autochtonous, however, evidence of a definitive clinical confirmation of these cases has not been given. In endemic areas of Japan (i.e. nearly the entire territory of Hokkaido Island and Rebun Island), *E. multilocularis* circulates between foxes, stray dogs, and voles (Yamashita, 1973); cats were occasionally found infected but there is no evidence that they participate in human contamination. *Clethrionomys rufocanus*, *C. rutilus* and, more recently, *C. rex* have been identified as the main intermediate hosts involved in the cycle in nature (Takahashi *et al.* 1989; Takahashi & Nakata, 1995). Horses, rats and especially pigs, raised in farms and fed with contaminated grass, were also found infected but their role in the natural cycle is doubtful.

People's Republic of China

The People's Republic of China (PRC) is a newly recognized focus of AE in Asia. Human AE cases were first recognized in Xinjiang Uygur Autonomous Region (XUAR) and Qinghai Provinces (QP) at the end of 1950s and infected animals were first reported from Ningxia in central China and north-east of Inner Mongolia in the 1980s (Li *et al.* 1985; Tang *et al.* 1988). To date, eight provinces or autonomous regions in China have been found endemic (Ito *et al.* 2003) (Fig. 2). *E. multilocularis* appears to occur in three areas: (1) Northeastern China (northeast focus): including Inner Mongolia Autonomous region (IMAR) and Heliongjiang Province (HP) (mainly

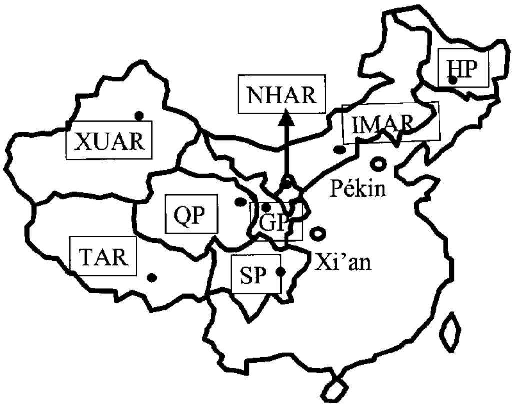

Fig. 2. Provinces and autonomous regions of PR China where alveolar echinococcosis is endemic. GP: Gansu Province; HP: Heilongjiang Province; QP: Qinghai Province; SP: Sichuan Province; IMAR: Inner Mongolia Autonomous Region; NHAR: Ningxia Hui Autonomous Region; TAR: Tibet Autonomous Region; XUAR: Xinjiang Uigur Autonomous Region.

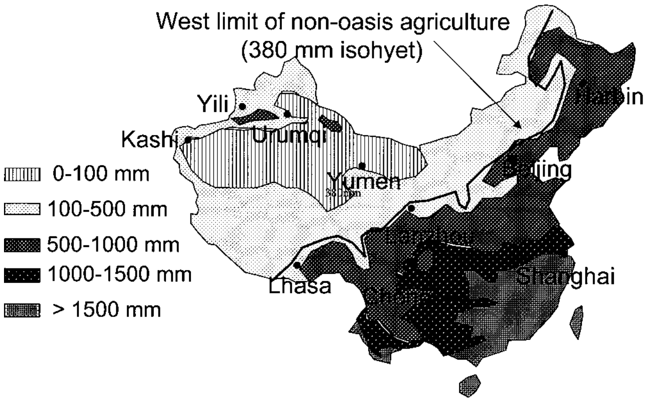

Fig. 3. Climatic map of PR China. Numbers art mean annual rainfall in mm.

covers the area of Hulunbeier Pasture, Da-xing-an-ling, Xiao-xing-an-ling mountains at the border with Russia and Mongolia). (2) Central China (central focus): including Gansu Province (GP) (mainly southern part on the confluence area of Qinghai–Tibet plateau and Loesis plateau): Ningxia Hui Autonomous Region (NHAR) (mainly Liupan mountains area in southern part on the Loesis plateau); Sichuan Province (SP) (mainly in Ganzi, Arba prefecture on Qinghai–Tibet plateau); Qinghai Province (QP) and Tibet Autonomous Region (TAR) (mainly at the border area with GP, SP) on Qinghai–Tibet plateau. (3) Northwestern China: including Xinjiang Uygur Autonomous Region, especially in Altai, Western Junggar and Tianshan mountains, Pamir Plateau bordered with Mongolia, Russia, Kazakhstan and Kyrgyzstan. The known foci are all situated in the mountainous areas covered with grassland or steppe, but no epidemiological details are available to make the distribution limits of the three foci in PRC more precise. Considering the climate and land-use pattern in China, the location of endemic areas likely overlap the places with annual precipitation of 300–500 mm and grassland (Fig. 3). The distribution range of *E. multilocularis* approximately fits the areas close to the 380 mm isohyet (Western Limit of non-oasis agriculture line) where mountain pastures, river canyons and steppe are typical landscape, and terraced farmland has been extended to the valley of lower altitude during the past five decades. The social and economic conditions within these areas are comparable; for instance, poor economic condition, isolated communities of minority ethnic groups with Muslim or Buddhist religions, animal herding with little agriculture. Although Xinjiang is far towards the west from the isohyet, its mountain areas have similar climate and social economic conditions as other endemic areas. The enzootic areas likely occur only in the areas of grassland, steppe and scrubland landscape at certain altitude with annual rainfalls more than 300 mm and mean temperature lower than 20 °C in July. The exact correlation between landscape, climate conditions and *E. multilocularis* distribution in China still requires appropriate studies which are currently being undertaken by several coordinated Chinese and international research multidisciplinary teams (Ito *et al.* 2003). Table 3 gives a summary of prevalence rates of AE in humans in central China, based on community surveys using ultrasound imaging and serology. The following description of AE in humans in the eight provinces or autonomous regions of PR China involved gives a synthesis of all sources available in international and Chinese literature together with some unpublished data obtained in the most recent studies in this area.

Heilongjiang Province (*HP*). HP (43°20′–53°20′N, 122°10′–135°5′E), located in the most northeastern part of China, shares the border with Russia by Heilong River to the north. It covers an area of 460 000 square kilometres with a population of 35 570 000 (the population density is 77·33 per square kilometre). Mean annual precipitation is 400–700 mm. Four human AE cases have been documented in three counties of the province (Yu *et al.* 1994). Cases from Nahe County and Jamusi City were reported respectively (Li *et al.* 1985; Wen, 1990). These two cities are close to Da-xin-an-ling and Xiao-xin-an-ling mountains where deforestation and farmland extension were noted as early as the 1950s (Xia, 1996). No data are available on animal infection and the characteristics of the local cycle of the parasite are unknown.

Inner Mongolia Autonomous Region (*IMAR*). IMAR (37°–54°N, 97°–126°E) covers an area of 1 100 000 square kilometres with a total population of 22 170 000. The region is bordered with Mongolia to the north and Russia to the northeast. The main

Table 3. Prevalence rates of alveolar echinococcosis in humans in central China (based on community surveys; cases were diagnosed with ultrasound and/or serological test)

Source	Wang *et al*. (1991)	Craig *et al*. (1992, 1997)	
Location	Liu-pan Mountains on the Loesis Plateau	Qinghai–Tibet Plateau	
Province	Ningxia Hui Autonomous Region	Gansu Province	
Prefecture	Guyuan Prefecture	Dingxi Prefecture	
County	Xiji 5·90% 141/2389	Zhang 4·95% 65/1312	Zhang & Ming 3·4% 84/2482
Sex			
Female	6·67% 90/1349	7·79% 47/603	4·83% 52/1077
Male	4·90% 51/1040	2·54% 18/709	2·82% 32/1402
Occupation			
Farmer	9·70% 137/1413	4·95% 65/1312	3·34% 83/2482
Herdsman	no	no	
Others	0·41% 4/976	no	
Ethnicity			
Han	5·1% 73/1433	4·95% 65/131	3·4% 84/2482
Hui	7·11% 68/956	no	no
Tibetan	no	no	no
Age range	19–72	11–73 (40·9)	12–70 (38·7)
Diagnostic methods	Ultrasound + ELISA	Ultrasound + ELISA	Ultrasound + ELISA
Peak value Age group	25–55	31–50	
Survey year	1988	1991	1994–1997

Source	Qiu *et al*. (1999); Schantz *et al*. (1998); Liu *et al*. (1998)					
Location	Qinghai–Tibet Plateau					
Province	Sichuan Province			Qinghai Province		
Prefecture	Ganzi Tibetan Prefecture			Yushu Tibetan Prefecture		Huangnan Tibetan Prefecture
County	Shiqu 2·96% 37/1251	Shiqu & Gahnzi 1·9% 76/3999	Ganzi 1·42% 39/2748	Gengduo 2·96% 37/1251	Yushu 2·03% 8/394	Zeku 0·29% 3/1046
Sex						
Female	5·27% 30/569	2·62% 45/2080	no data	no data	no data	0·29% 3/1046
Male	no data	1·62% 31/1919	no data	no data	no data	no data
Occupation						
Farmer	no data	1·14% 6/526	1·35% 7/520	no data	no data	no data
Herdsman	6·59% 27/410	5·44% 44/809	3·19% 10/313	2·12% 12/565	no data	no data
Others	no data	0·98% 26/2664				
Ethnicity						
Han	no data	no				
Hui	no	no				
Tibetan	no data	1·90% 76/3999				
Age range	13–81 (45·6)					
Diagnostic methods	Ultrasound + ELISA			Ultrasound + ELISA		
Peak value Age group	no data			no data		
Survey year	6/1997–8/1998			1997–1998		

inhabitants are Mongols with herding activities. The annual precipitation is 80–450 mm (higher in east and lower in west). One male case from Hulunbeier pasture was reported in 1987 (Ji, Xing & Xu, 1987). The case lived in Chen-bai-hu-qi where infected rodents were recorded (Tang *et al*. 1988). Although more human AE cases were diagnosed in the province, according to local reports, no more cases were formally published from this region. Corsac foxes were found infected in this area; *Microtus brandti* (a cyclic species) and *Meriones unguiculatus* have been recorded as naturally infected, but other small mammals from the rodent and lagomorph families (e.g. *Ochotona daurica*) are present and may also serve as intermediate hosts.

Ningxia Hui Autonomous Region (*NHAR*). NHAR (35°14′30″–39°23′N; 104°17′–107°38′50″E), located on the Loesis in central China, covers an area of 66 000 square kilometres with a population of

5 040 000. One third of inhabitants are Hui Muslims with farming activities. Annual precipitation is between 200 and 600 mm; it is higher in Liupan Mountains in the southern area connected to Gansu province and lower in the northern area connected to Inner Mongolia Autonomous Region. Human AE cases were found in three counties (which belong to Guyuan Prefecture): Xiji, Haiyuan and Guyuan Counties in the Liupan Mountains area, in southern NHAR (Lin & Hong, 1991; Wang *et al*. 1991). Up to 1989, 304 human AE cases from XHG were diagnosed (E.P.S.N.R., 1999). A community mass-screening survey was conducted in Xiji County in the 1980s (Wang *et al*. 1991). A total of 2389 subjects from two villages (Xinyeng village with a majority of Han people, and Bai Ai village with a majority of Hui people) and one town (Xiji county city, civil servants) were examined with ultrasound and serological tests (ID and ELISA). A total of 141 human AE cases were diagnosed as AE by ultrasound and confirmed by serological tests (prevalence rate 5·9%). The age of infected people ranged from 19 to 72 years. No significant differences of prevalence were observed between sexes and ethnic groups, but a higher prevalence (9·7%: 137/1413) was recorded in farmers living in rural areas and a lower prevalence in those living in cities (0·4%: 4/976) (Wang *et al*. 1991); 4 cases from the same family of 8 members were diagnosed. This family used to hunt ground squirrels (*Spermophilus* spp.) for meat and gave the raw viscera to their dogs. A community ultrasound screening in Yumu village (which belongs to Xiazhai community of Xiji County) showed a prevalence rate of AE of 4·6% (6/130) in this village (E.P.S.N.R., 1999). A total of 113 clinical cases diagnosed in Guyuan Hospital between 1965 and 1991 were reported (Mu & Sueng, 1991): mean age was 31 yrs, 80% of the patients aged from 20 to 40 yrs and the male to female ratio was 1·1 : 1. Preliminary results of a mass screening performed in 2114 subjects living in the northern area of Xiji county in 2002 showed an overall prevalence of 2·4%, with a prevalence over 6% in 3/9 communes (Nan Wen, Bai Ai and Zhuang Cun Pu). (P. S. Craig and Yang Yurong, personal communication). The mean and lower age of the patients disclosed with AE lesions suggest that patients were infected more than 20 years ago and that the local parasitic cycle could have been interrupted after dog populations dramatically declined following campaigns to kill rodents using anticoagulant drugs at the beginning of the 1990s. Infection of red fox (*Vulpes vulpes*) in this province in 1985 by Li and co-workers was the first report of animal infection by *E. multilocularis* in China. Dogs were likely involved in transmission to humans in the rural communities of south Ningxia in the past (Rausch, 1995; P. S. Craig, personal communication); however no dog infection has formally been identified. Infected *Spermophilus dauricus* and *S. alashanicus* were found in 1985 (Li *et al*. 1985), both *Spermophilus* spp. and *Myospalax fontanieri* were infected with fertile cysts containing protoscolices in 1987 (Hong & Ling, 1987), though experimental infection in the genus *Spermophilus* has generally shown a poor fertility of cysts (Rausch, 1995; Zhou *et al*. 1998). *Ochotona* spp., lagomorphs involved in *E. multilocularis* transmission in other provinces, were not infected in this autonomous region. Other suitable intermediate hosts such as *Cricetulus* spp. and *Meriones unguiculatus* were recorded in scrub-grassland in Liupan Mountains (Wang, 1989); evidence of infection by *E. multilocularis* is, however, missing from parasitological reports. The situation of northern Ningxia, close to Inner Mongolia, regarding AE in humans is not clear: no human cases were spontaneously reported in this area.

Gansu Province (*GP*). GP (32°30′–42°47′N, 92°13′–108°40′E) has border with NHAR towards northeast, SP towards south, QP towards west; it covers about 390 000 square kilometres of area with a population of 23 520 000. Mean annual precipitation is 40–800 mm (lower in west and higher in southeast). Human cases were recorded only in southern GP. The first community mass screening performed at the end of the 1980s in Zhang County of Dingxi Prefecture revealed that a serious public health problem occurred in this province (Craig *et al*. 1992). Prevalence rate in humans averaged 5% (65/1312) and was significantly higher in females than in males. This high prevalence was attributed to infected dogs combined with poor hygienic conditions (Craig *et al*. 1992). In 1994, a collaborative Chinese, British and French study was initiated to better understand the epidemiology of the disease in this area. An ultrasound mass screening (with serological confirmation) carried out in Zhang and Ming Counties between 1991–1997 revealed that prevalence rates ranged between 0–16% in villages and a peak value of 16% was recorded within a small region (20 km radius). Overall mean prevalence was 4% (135/3331) within the two connected counties (Zhang and Ming) (Craig *et al*. 1992, 2000; Bartholomot *et al*. 2002). Among 2482 subjects from 28 villages, a typical lesion of progressive AE was disclosed in 84 subjects; in addition various types of calcifications were observed in the liver of 451 examined subjects, suggesting a high prevalence of 'abortive cases'. Females found with AE lesion were more frequent than males: 52 women and 32 men, mean age 38·7 yrs (extremes 12–70 yrs). This seems to reflect special conditions of human contamination, with dogs as an important definitive host, and more frequent contact of children and women with these dogs. In fact, dogs seem to play (or to have played) a major role in human contamination. Six of 59 dogs examined (10%) were found infected in Zhang County. Numbers of *E. multilocularis* worms in dog intestines ranged from 20 to 5000 worms (Shi, 1995; Craig *et al*.

1992). Wolf, red fox, corsac fox (*Vulpes corsac*) and Tibetan fox (*V. ferrilata*) are present in Gansu. Only the red fox, and very rarely the wolf, were believed by farmers to be present in the study area of Zhang and Ming counties where the highest prevalence of AE in humans was found; however they were not systematically studied for *E. multilocularis* infection (Zhang, 1997). An ecological survey of small mammals in the endemic area has shown that the deforestation which occurred twenty years ago had resulted in the succession of small rodent communities in this area (Giraudoux *et al*. 1998). Shrub-lands and pastures, a vegetation stage occurring after deforestation, might have supplied favourable habitats for susceptible species such as *Microtus limnophilus* and thus enhance *E. multilocularis* transmission dynamics in this area (for a review, see Giraudoux *et al*. 2002, and Giraudoux *et al*. in this supplement). However, no formal demonstration of infection of the various small mammal species present in the area has ever been given. Transmission to humans may well have been interrupted in this region: because of massive deforestation, the populations of wild carnivores have markedly decreased: foxes have been rarely seen in the past ten years; and the local villagers confirmed that dogs were eliminated at beginning of the 1990s; as in Ningxia autonomous region, dogs as well as foxes might have been killed by secondary poisoning during rodent-control campaigns. It is thus unlikely that active transmission still occurs in this area which had the highest prevalence of AE ever reported in the world. In fact, taking the population size in the two counties into account, the prevalence rate may be estimated to be 200 per 100 000 inhabitants in comparison to 65 per 100 000 in St Lawrence (Alaska), 10 per 100 000 in Franche-Comté (eastern France) or in northern Switzerland (Schantz *et al*. 1995; Bresson-Hadni *et al*. 1997; Eckert, 1997).

Qinghai Province (*QP*). Qinghai Province (31°30′–39°30′N; 89°30′–103°40′E) is located totally on the Qinghai–Tibet plateau. It covers the area of 720 000 square kilometres with 4 610 000 inhabitants. Mean altitude is 3000 m with summer pastures above 4500 m. Most areas are covered with steppe pastures for animal husbandry and bare ground. Farmland only occupies small areas close to Xining City (capital of the province) at a lower altitude. The mean annual precipitation is about 100–600 mm. Human AE cases were discovered at the end of 1950s and the first clinical report from this province was published in 1964 (Liu & Qu, 1964). This is probably the earliest report of a human AE case in China. The first reported patient was 22 yr-old man who died of AE brain metastases in 1959. Twenty cases of liver AE were reported from the same hospital. Qinghai Endemic Disease Control Office has reported 143 cases of AE coming from 18 counties over the province, diagnosed from 1980 to 1992. Most cases lived in the south-eastern part where herding is the main activity (Wang *et al*. 1999). Epidemiological information is available from a community screening (by ultrasound) carried out in Yushu Tibetan Prefecture (including Yushu and Chengduo counties which are close to Sichuan Province) and in Huangnan Tibetan Prefecture (Zeku County which is close to Gansu Province) in 1997 and 1998. The prevalence rate in humans was of 2·0% (8/394) in Yushu County, 1·52% (19/1253) in Chengduo County, and 0·29% (3/1046) in Zeku County (all 3 cases were Tibetan women) (Liu, Qiu & Schantz, 1998; Schantz, 1998). Two out of fifteen feral dogs (13·3%) in Chengduo County of Yushu Tibetan Prefecture were found to be infected in 1994 (Schantz, 1998); 3/9 foxes (*Vulpes corsac* and *V. ferrilata*) were found infected in Haibei Prefecture (Wang *et al*. 1999). Naturally infected *Ochotona curzoniae*, ‘pikas’, have been reported in this province (Guo, 1986; Wang *et al*. 1999; Liu *et al*. 1998; He, Han & Wu, 1994). Very high prevalence rates of 3·5% were found in Huangnan Tibetan Prefecture (Wang *et al*. 1999), 3·5% to 7·7% in Yushu County and 3·5% in Chengduo County of Yushu Tibetan Prefecture (Liu *et al*. 1998; He *et al*. 1994). *Ochotona* has been reported as the main pest on the alpine meadows of this region (Wang, 1996). One hare (*Lepus oiostolus*) in Huangnan Prefecture, 18/384 yaks and 31/578 sheep were also naturally infected with *E. multilocularis* in this area (Wang *et al*. 1999); however, these species are unlikely involved in the maintenance of the parasitic cycle. It is, conversely, likely that the parasitic cycle responsible for human infection involves all 3 species of foxes (including *Vulpes ferrilata*) present in the province as well as feral dogs, and *Ochotona curzoniae*, which are known to serve as prey to foxes and dogs as well (Liu *et al*. 1998; Schaller, 1998). Microtine species (noticeably *Microtus oeconomus*) are widely spread on the plateau and may also be involved locally. The dog population is steadily increasing especially in Buddhist communities for religious reasons. Wolves may also be involved in the parasite cycle: Schaller (1998) reported that they preyed heavily on marmots and *Ochotona*.

Sichuan Province (*SP*). SP (26°–34°40′N, 97°30′–108°30′E) covers areas of 478 000 square kilometres with a population of 80 820 000 (Chongqin city, which became an independent metropolis in 1997, not included). It is one of the provinces with the highest population density in China. Its western part is located on Qinghai–Tibet plateau and bordered with Tibet, Qinghai and Gansu Provinces. Mean annual precipitation ranges from 500 to 1200 mm. Human cases of AE were only identified in Arba and Ganzi Tibetan Autonomous Prefectures located on the Qinghai–Tibet plateau. In these two autonomous prefectures, human cases were found in Shiqu, Derger, Ganzi, Seda, Kangding and Nuoergai counties

(Lin & Hong, 1991; Qiu, Liu & Schantz, 1999). The areas where AE cases have been documented are endemic for both AE and cystic echinococcosis (see Schantz *et al*. in this supplement). An epidemiological survey of echinococcosis (including AE and CE) in Ganzi and Shiqu County of Ganzi Prefecture was undertaken between June 1997 and July 1998. Among 3999 subjects from 8 communities (36°19′–31°24′N; 97°20′–100°25′E) who were screened using B-ultrasound, X-ray and Dot-ELISA, 76 AE cases were diagnosed which represents a prevalence rate of 1·9%. In Shiqu County where most of the landscape was dominated by pastures and populated with pastoralists, the mean prevalence rate nearly reached 3% of the total population and 6·6% in the herdsmen population (most of them are Tibetan). In Ganzi County, where semi-pasture and semi-agriculture areas are present, the mean prevalence was 1·4% in the total population, and 3·2% in herdsmen (Qiu *et al*. 1999; Liu *et al*. 1998). The prevalence rates were statistically different between the two counties. Potential risk factors for human infection with *E. multilocularis* were analysed: the prevalence rate was strongly and positively linked with low economic income of the family, drinking pool water rather than tap water, dog ownership, fox pelt ownership (Qiu *et al*. 1999; Wang *et al*. 2001). Surveys on *E. multilocularis* in wildlife at Ganzi Tibetan Prefecture (including Shiqu and Ganzi Counties) from 1983 to 1997 revealed prevalence rates of 57% in red fox, 59·1% in Tibetan fox, and 17% in feral dogs. High prevalence rates of *E. multilocularis* were found in *Microtus irene* (up to 25%), *Ochotona curzoniae* and *Lepus oiostolus* (Qiu *et al*. 1999). Several species of livestock were also infected with *E. multilocularis* such as yak, sheep (3·1%) and pigs. Due to the concomitant presence of both *E. multilocularis* and *E. granulosus* in this area, misidentification of the lesions is possible; however, the substantial number of livestock reportedly infected with *E. multilocularis* both in Qinghai and Sichuan Provinces, by researchers well aware of the parasitological characteristics of both *Echinococcus* species, is puzzling and needs further confirmation using molecular characterization of the species.

Tibet Autonomous Region (*TAR*). Like Qinghai Province, Tibet Autonomous Region (26°30′–36° 30′N, 78°–100°E) is entirely located on the Qinghai–Tibet plateau and covers an area of 1 200 000 square kilometres with a population of 2 320 000. The population density is the lowest in China (1·9 inhabitants per square kilometre). Annual precipitation ranges 200–500 mm. Some areas can reach 2000 mm in south TAR (Himalaya Mountains area). Fourteen human AE cases have been documented in the northeast part of Tibet (Changdu and Naqu Prefectures) near Qinghai and Sichuan Provinces (Peng, 1988; Yixi, 1992; Luo, 1993; Pu, 1999). Ten clinical AE cases were reported from People's Hospital of Tibet in Lhasa (Yixi, 1992). No more information on epidemiology in humans, especially from systematic surveys, is available. Feral dogs were infected with *E. multilocularis* in eastern TAR close to Sichuan Province (F. J. Liu, personal communication). *Ochotona* is the dominant genus of small mammal in the pasture areas and also a main prey for Tibetan foxes (Schaller, 1998). To date no more investigations on *E. multilocularis* cycle in this region have been reported.

Xinjiang Uygur Autonomous Region (*XUAR*). XUAR (34°32′–49°31′N, 73°32′–96°21′E) in northwestern China covers an area of 1 600 000 square kilometres with a population of 16 050 000 inhabitants. It is the largest province (or autonomous region) of China. Mean annual precipitation ranges from 20 to 500 mm (higher in north and lower in south). It shares a border, from northeast to southwest, with Mongolia, Russia, Kazakhstan, Kyrgyzstan, Tajikistan, Afghanistan, Pakistan and India. Except for Afghanistan and Pakistan, most of the former USSR countries bordered with Xinjiang are known to be endemic for *E. multilocularis* (Bessonov, 1998).

In 1956, the first human case (a 33 yr-old Kazakh male) from Yili valley was hospitalized in the first affiliated hospital of Xinjiang Medical University (formerly Xinjiang Medical College) in Urumqi. This case was not diagnosed clearly until the second patient (a 24-yr old Kazakh female) was seen in the same hospital in 1958. The first 6 clinical cases diagnosed in this hospital were reported in 1965 (Yao *et al*. 1965). After then, new cases have been diagnosed regularly in the same hospital: 52 clinical cases from the whole region were reported in 1986 (Yao *et al*. 1986). However, in most reports, little information on epidemiology is available (Yao *et al*. 1965, 1986; Wang, 1978), and until the end of the 1990s, endemic areas were considered to be located along central Tianshan mountains and Kazakhstan border (Schantz *et al*. 1995). Epidemiology of AE in XUAR has been updated in 2000 by the analysis of data collected from the medical records of 157 clinical cases, all diagnosed after 1980, who had attended the four main hospitals in the region (in Urumqi, Yili, and Karamay) where imaging equipment available after 1980 has made correct identification of cases possible (Zhou *et al*. 2000). These data indicate that the disease is relatively common in the Altai, western Junggar, and Tianshan mountain ranges, whereas the Tarim and Junggar basins are likely to be of low endemicity. The highest prevalence (3·9/100 000) was observed in the Altai mountain zone. The prevalence of the disease in the Kunlun Mountain appears low but could have been underestimated. Semi-nomadic groups, especially those of Kazakh and Mongol origin, have a higher risk of infection than other ethnic groups. However changes in the

Table 4. Alveolar echinococcosis in humans; annual incidence rates of symptomatic cases per 100 000 inhabitants, and asymptomatic AE cases found at mass screenings, from published data

Country	Period	Incidence	Reference
Austria			
Whole country	1983–1990	0·02	Auer & Aspöck (1991)
France			
Franche-Comté	1971–1988	0·5	Bresson-Hadni (1988)
Dépt du Doubs	*1960–1992*	*1·4*	*Bresson-Hadni et al. (1994)*
Dépt du Doubs, mass screening (dairy farmers)	*1987–1992*	*8/7, 884*	*Bresson-Hadni et al. (1994)*
Franche-Comté	1983–1998	0·7	Bresson-Hadni *et al.* (2000)
Germany			
Bavaria	1985–1989	0·03	Nothdurft *et al.* (1995)
Baden-Württemberg, mass screening (endemic village)	*1997*	*3/2, 560*	*Romig et al. (1999)*
Switzerland			
Whole country	1970–1983	0·18	Gloor (1988)
Whole country	1984–1992	0·10	Eckert *et al.* (1995)
Canton du Jura	*1970–1983*	*0·74*	*Gloor (1988)*
Western Switzerland, mass screening (blood donors)	*1986*	*2/17, 166*	*Gottstein et al. (1987)*

In italics: studies performed in limited areas where average fox infection by *E. multilocularis* reaches 50%.
Number of AE cases/number of screened subjects in endemic areas is given for mass screenings.

behaviour of communities, and especially sharing of winter settlements with Han sedentary communities, could also change epidemiological features of the disease in the endemic areas. Prevalence of the disease appears to be correlated with aspects of the local climate such as relatively high annual precipitation (higher than 400 mm) and low temperatures (averaging −22 °C in January and 17 °C in July). In four Counties (Ermin, Toli, Tacheng and Yumin counties) in Western Junggar Mountain at the border area with Kazakhstan, adult *E. multilocularis* were found in 11 of 36 red foxes and 1 of 2 wolves. The role of dogs in the transmission to humans is doubtful: Liu (1993) noted that a total of 27 186 dogs had been examined for the presence of *Echinococcus* spp. after autopsy from 1957 to 1991 in Xinjiang: no occurrence of *E. multilocularis* was reported in dogs by investigators. Except very few reports of naturally infected *Mus musculus* and *Spermophilus erythrogenys* without protoscoleces, which still have not been confirmed, no formal identification of the small mammals involved in the parasite cycle in XUAR has been done. Bone remains of *Marmota* were found in dog faeces collected from the western Junggar mountains in July 1996, and the Altai mountains in 1998 (Zhou, 2001); this suggests that dogs could also be involved in human transmission in this region. Microtines, *Ochotona* spp., and *Marmota* spp., which are abundant in mountain areas and were reported as prey for foxes and wolves in the Kunlun mountain (Schaller, 1998), could well serve as intermediate hosts and contribute to maintain the local natural cycle, as well as species of cold semi-desert as *Allactaga* spp., *Dipus* spp., *Cricetulus* spp. and *Meriones* spp. Actually, small mammal communities, landscape and ecological conditions may be very diverse within some hundred kilometres. The respective role of each community regarding sustainable transmission still remains unknown.

ALVEOLAR ECHINOCOCCOSIS IN EUROPE

Western Europe

Some incidence rates from European countries based on well documented published studies up to the beginning of the 1990s are summarised in Table 4. The average incidence rates, referred to the total population of a country, are rather low: 0·18 (1970–1983) and 0·10 (1984–1992) cases per 100 000 inhabitants per year in Switzerland; 0·02 and 0·03 in Austria and Bavaria in Germany. However, locally, because of the geographically-focused nature of the parasitic cycle, the incidence rates may be higher, for example in the Canton du Jura in Switzerland with 0·74, or in the Département du Doubs in France with 1·4. This has to be taken into account when examining the actual risk in a given European region. Between 1980 and 2000, autochthonous human cases of AE have been documented and published from several European countries, namely Austria, France, Germany, Switzerland and the European part of Turkey (see Bresson-Hadni *et al.* 1988, 1997, 2000; Stössel, 1989; Vuitton *et al.* 1990; Schantz *et al.* 1995; Ammann & Eckert, 1995; Eckert, 1997; Eckert & Deplazes, 1999; Eckert *et al.* 2001). The number of verified and published cases from Europe (Austria, France, Germany and Switzerland) between 1900 and 1980 amounted to 844 cases (Fesseler, 1990). Sporadic ‘imported’ cases were described from Belgium (Claudon, 1983). A systematic recording

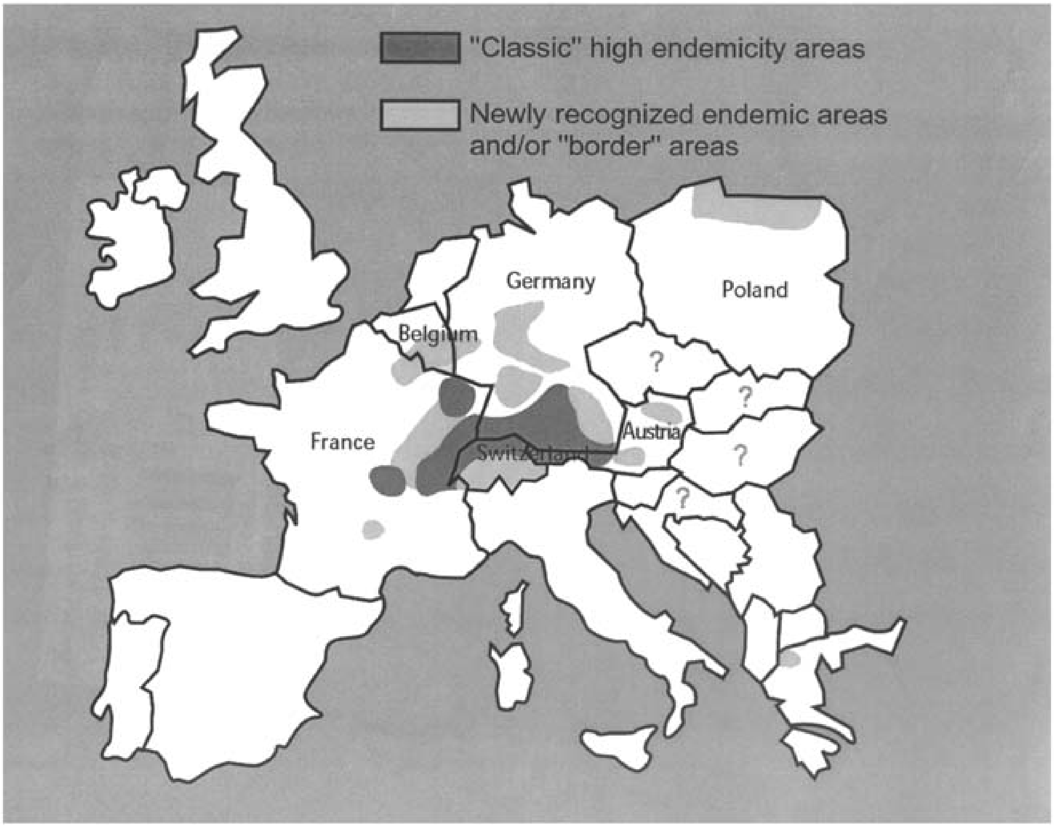

Fig. 4. 'Old' and 'new' endemic areas for human alveolar echinococcosis in Europe (adapted from the geographic location of human cases, according to Kern *et al.* (2003); data from the EurEchinoReg).

of cases was only done in Switzerland in the past 20 years, until 1997, and most of the reports in the various countries of Europe were based on hospital collection of cases, single case reports and not on a systematic epidemiological study. Systematic mass screenings were performed in endemic areas of Switzerland (Gottstein *et al.* 1987), southern Germany (Romig *et al.* 1999; Jensen *et al.* 2001), and eastern France (Bresson-Hadni *et al.* 1994).

A consortium of European research teams involved in the management of AE cases undertook the establishment of a European registry of alveolar echinococcosis cases (EurEchinoReg) in 1998 and thus allowed a more accurate collection of human case data. Data collected from January 1982 up to August 2001 were recently published (Kern *et al.* 2003). From 1982 to 2000, a total of 559 AE cases from Western and Central Europe were reported to the Registry; 258 patients were males (46%), 301 were females (54%) (Gender ratio 1:1·2). The median age at first diagnosis was 56 years (mean 52·5, range 5 to 86 years) and was almost equal in men and women. Proportion of patients under 20 years was 2% (121/559) and of patients over 69 years 16% (88/559). By December 2000, 73·0% of the patients, whose diagnosis was ascertained in 1982 and afterwards, were alive, 21·3% had died and 5·7% were lost to follow-up. For countries of the European Union and Switzerland, there were 53 autochthonous cases of AE in Austria (highest annual incidence: 6), 3 in Belgium (diagnosed in 1997 and 1999), 235 in France (42%; highest annual incidence: 26), 126 in Germany (24%; highest annual incidence: 20), 1 in Greece, and 112 in Switzerland (21%; highest annual incidence: 11). For most of the 530 autochthonous cases, the residences correspond most closely to the area of infection. A complete documentation of the residences during the patients' whole lifetime was available for about 30% of patients. Mobility of this patient subgroup was low, obviously in conjunction with long-term farming. Among the 15 'imported' cases reported by the various European centres, 7 originated from neighbouring countries and 8 from central Asia.

The number of incident cases per year varied between years with a peak incidence of 36 patients in 1988; notifications ranged between 15 and 27 patients. The median numbers of patients reported to the registry per year did not vary during the two decades under study (1980s: 24; 1990s: 22). Thus, low but constant incidences are characteristic of the occurrence of human AE in Europe today. Under-reporting from previous years can be responsible for an apparent increase of incidence in Germany (Lucius & Bilger, 1995); conversely, under-reporting since 1998 may explain a decline in Switzerland. Mass screenings performed at the middle of the 1980s in the endemic areas of Franche-Comté (east of France at the border with Switzerland), which disclosed several cases within 5 years and more generally raised the awareness of the disease in this region, might explain the observed increase in the number of cases in France.

Improved diagnostic technology (ultrasound examination of the liver, CT-scan, MR-imaging as well as improved serological tests) has taken place in Europe since the beginning of the 1980s, and has probably led to an optimal detection rate. This could explain why more than 500 cases have been reported for these 2 decades, while less than 900 cases were published for the previous 7 decades. Nevertheless, changes in animal infection and in risk exposure for humans cannot be excluded totally. Information on potential risk factors was available for 38% patients from Austria, Germany, Greece and France, 97 men and 113 women. Twenty two percent were farmers; 46·2% of the patients with other professions, housewives and students were regularly engaged in farming, gardening or related activities as a pastime, as well as 62% of pensioners and unemployed. A majority of the patients (70·5%) had owned or formerly kept dogs and cats. Among the pet owners, 105 persons were also actively farming or gardening. Only 15 patients (7·1%) were neither farming nor gardening and did not own pets. In Europe, only one case-control study including 21 patients and 84 controls from Austria has been published (Kreidl *et al*. 1998). A high association of the disease was found with cat ownership and hunting, but due to the low case number the study was of limited power. Farming did not seem to have an impact on infection risk. However, comparisons of professions in an endemic area of Eastern France have shown that farmers were over-represented among patients with AE, compared with the proportion of farmers in the same area (Vuitton *et al*. 1990; Bresson-Hadni *et al*. 1997). A case-control study that involved 100 highly seropositive subjects found at mass screening in eastern France as cases, and 200 seronegative subjects matched for age, gender and place of residence as controls did not find any significant relationship with hunting, owning dogs or eating dandelions, but a significant association with frequent consumption of non-cooked berries collected in nature (Vuillemin, 1997). Data from the European registry on occupational and recreational activities among patients suggest a high frequency of putative exposure (farming, gardening, owning dogs and cats) but the lack of a comparison group does not allow an evaluation of the risk potential of these behaviours. They may be characteristic for the majority of the population from rural communities in Europe, as indicated from the preliminary results of a sociological study which is being performed in Eastern France (D. Jacques-Jouvenot, personal communication). Individual cases point to very specific factors of contamination, such as keeping a fox as a pet (Bresson-Hadni *et al*. 1988). However, for Europe, the question of how risk behaviour could be defined and how exposure can best be prevented is, therefore, still unclear.

Most residences are clustered in defined regions: central France, Lorraine, French Jura and Savoy, Swiss Jura and Swiss northeast, southern Germany, and western Austria. Single cases were identified in Belgium, in the northern regions of France, Germany, and in northeastern Austria (Fig. 4). The patient from Greece lived in the Greek province Macedonia. The distribution of AE in Europe shows high densities of cases in the classic endemic regions in Austria, France, Germany, and Switzerland. These regions are those where the index cases from each of these countries were identified since 1855 (Fesseler, 1990). In areas at the border of these 'classic endemic regions', clusters of a few patients or single cases were observed. In the well-known endemic areas, recent screening studies detected not only a small number of patients with the disease (12/12 000 subjects screened using serology followed by ultrasound and/or CT-scan examinations in Franche-Comté, France, from 1987 to 1994) (Bresson-Hadni *et al*. 1994, 2000), but also self-cured infections, also called 'aborted lesions', first described by Rausch *et al*. (Rausch *et al*. 1987). Such 'aborted lesions' were also disclosed in China (Bartholomot *et al*. 2002), as well as seropositivity rates of up to 2% in various endemic areas (Bresson-Hadni *et al*. 1994; Romig *et al*. 1999; Gottstein *et al*. 2001). Fifteen persons with aborted hepatic lesions (lesions with characteristic calcifications) and positive serology were notified to the Registry. They are not included in the numbers reported above. Together with a persistent *E. multilocularis* seroprevalence in the screened populations, they point to a previous contact with the infectious agent and to a high level of 'infection pressure' in the endemic areas. They also show that transmission of *E. multilocularis* to humans occurs rarely, and that incidence of the disease is far lower than exposure of the 'at risk' human communities to the parasite (estimated to 1/10). Genetic susceptibility, especially related to genes within the Major Histocompatibility Complex (Eiermann *et al*. 1998; Zhang *et al*. 2003), plays a role in the actual emergence of the disease in human population, and various levels of tolerance towards *E. multilocularis* may explain the spectrum of immunological interactions between the larva and its human host (Godot *et al*. 1997, 2000*a*, *b*) and thus the spectrum of clinical expression of the disease (Bresson-Hadni *et al*. 1997, 1999). Acquired immunodeficiency, such as AIDS, therapeutic immune depressants or, to a lesser degree, young age or pregnancy may also promote parasitic growth and clinical symptoms (Seiler *et al*. 1997; Vuitton *et al*. 2002; Kern *et al*. 2003). This has obvious consequences when considering the epidemiology of the disease in humans and its counterpart in the animal hosts (Vuitton *et al.* 2002).

In most European endemic areas the transmission cycle is predominantly sylvatic involving red foxes as definitive hosts and arvicolid rodents, mainly *Arvicola terrestris* and *Microtus arvalis* as intermediate hosts. Prevalence of the disease in a given region of Eastern France has been shown to be significantly correlated to the occurrence of high densities of *A. terrestris* in the same area (Viel *et al.* 1999). The risk of rodent population outbreaks are themselves related to land use, and particularly permanent pastures devoted to dairy cow breeding, in Europe (Giraudoux *et al.* in this supplement). Muskrats have also been found infected in Eurasia (Rausch, 1995); they were found infected in France and are likely to be much involved in the parasite cycle in Southern Germany; *E. multilocularis* infection rates in muskrats have been increasing within the past decade and may reach nearly 40% of trapped muskrats in some areas of Baden-Württemberg (Romig *et al.* 1999). Such high prevalence of *E. multilocularis* infection in rodents is rare. Except in very specific 'hot spots' (Giraudoux *et al.* 2001; Gottstein *et al.* 2001) where it can reach 40%, infection of voles by *E. multilocularis* has a low prevalence (Deplazes & Eckert, 2001; Giraudoux *et al.* 2002). Conversely, prevalence of infection in foxes is often over 60% in the highly endemic areas (Deplazes & Eckert, 2001; Raoul *et al.* 2002).

Central Europe

Sporadic, presumably autochthonous cases have been reported from the Czech Republic (Slais *et al.* 1979), Slovak republic (Krcmery *et al.* 1989), Poland (Pawlowski, 1996) and Greece (Theodoropoulos *et al.* 1978). Cases in Bulgaria have been reported in several publications collected by Genov, Silenov & Polydkova-Krusteva in 1980: in the absence of formal confirmation of these cases, and due to the high prevalence of cystic echinococcosis in this country, the actual presence of AE in this country cannot be ascertained. The same applies for Romania: among 638 cases of 'hydatidosis' collected during the period 1981–1990, lesions with multiple cysts were detected in 15% of cases: this, and the location of cases, might suggest that AE could be found in mountain shepherds in Romania (Coroiu, Rusu & Stefanoiu, 1992). One case was also reported from Hungary (Jakab & Faller, 1988). All references on single case reports and on the situation regarding animal contamination in central and Eastern Europe until 1999 can be found in a review by Kolarova (1999).

Collection of cases in central Europe countries was undertaken in association with the EurEchinoReg in Poland and in Czech and Slovak republics. Fourteen cases were collected in Poland (highest incidence: 4 cases per year). No cases could be formally confirmed for Czech and Slovak republics.

Preliminary results from the Echinorisk programme (Romig, for the Echinorisk programme, personal communication) show that 53% of foxes were infected in the Carpathian foothills in the south of Poland. This regional focus of transmission is mirrored by data from the bordering region of Slovakia, and appears to be of recent origin since a previous survey only five years ago showed a much lower infection rate of 8%. A general increase in prevalence rates, although less dramatic, was also observed in other regions of Poland. Infection of 5/100 foxes in Hungary was recently reported by Streter *et al.* (2003); all five infected foxes were shot in 2 northern counties of Hungary, in the Northern Mountain Range, at a distance of 60–120 km from the nearest known *E. multilocularis* endemic region, the Muránska Planina Mountains in Slovakia.

NEW EPIDEMIOLOGICAL TRENDS

Increase in fox population and in fox infection in Europe

Comparisons between prevalence rates measured in the 1980s and the end of the 1990s seem to indicate a significant increase, at least in two areas of Western Europe where suitable data were available (Romig, for EurEchinoReg, 2002). In Baden-Wurtemberg, southern Germany, large-scale monitoring showed that prevalence ranged from 0% to 30% in the period 1973 to 1984, and then ranged from 0% to more than 50% in the period 1995 to 1999 (Romig *et al.* 1999). In the plateau area of the Jura Mountain (France), prevalence in the Jura Département increased from 27% to 53% between the period 1981–1989 and the period 1996–1999, and prevalence increased from 46% to 65% in the Doubs Département (Raoul *et al.* 1999; Giraudoux *et al.* 2001). A similar increase was also observed in Belgium, province of Luxembourg, a rather recently identified endemic area (Losson *et al.* 1997), and it is worth noting that the first autochthonous Belgian human cases were found within the past 5 years (Kern *et al.* 2003).

A concomitant increase in fox populations has been observed in several countries of Europe since the beginning of the 1990s: regionally in Spain, Bulgaria, Sweden, France, Germany, Switzerland, Belgium and Czech Republic (Artois, 1997; Chautan, Pontier & Artois, 2000), a combination of rabies vaccination and modification in human-fox interactions (fox control, habitat changes) may account for higher survival and fertility (Chautan *et al.* 2000).

For the first time the presence of *E. multilocularis* in foxes has been reported in Italy, Bolzano Province, at the border of Austria (Manfredi *et al.* 2002). No infected foxes have been found at the French-Italian border, despite the presence of human cases in the French Alps. This is of specific significance for the definition of the southern limit of the parasite's range in Europe, and, together with data from Southern Switzerland and southern Austria, it provides an added opportunity to identify factors responsible for its absence in most Mediterranean regions. Preliminary results from the Echinorisk programme, a European Commission-sponsored project to assess the current risk factors of transmission to humans indicate that, for the first time too (Romig *et al.* report to the European Commission, personal communication), *E. multilocularis* was recorded in foxes from Burgenland, the easternmost federal state of Austria. Locally, the prevalence there was found to be up to 18%, while no infected fox was recorded in surveys ten years ago. Based on these results, transmission in eastern Austria appears to increase, and the occurrence of the parasite in bordering Hungary is likely. The latter is supported by the fact that *E. multilocularis* also occurred with moderate prevalence levels in Slovakia at the border to Hungary. The extension of the endemic area towards Scandinavian countries is also suggested by the presence of infected foxes in the Netherlands (Van Der Giessen *et al.* 1999) and by the discovery of an infected fox in the city of Copenhagen, Denmark (Petersen & Kapel, 2000; Saeed & Kapel, 2001). The specific problem of Great Britain, which is still considered as free of *E. multilocularis*, is particularly relevant since infected animals could enter the territory in the future because of suppression of the quarantine regulation. Studies on fox infections in England are currently being done within the Echinorisk programme mentioned above.

Urban foxes and the risk of AE in urban human populations

The continuing adaptation of wild foxes to living conditions in settlement areas and cities is on record from many areas in Western Europe, e.g. in Switzerland (Gloor *et al.* 2001). Infection of these 'urban foxes' by *E. multilocularis*, causes concern that a far bigger section of the human population might be at risk to contract AE than previously assumed. The current situation in Hokkaido and in the city of Sapporo shows that the risk is not only a possibility but a reality: an *E. multilocularis* coproantigen survey suggested the presence of the parasite in 58% of foxes from 19 den sites, most of these 'positive' dens being located in the peripheral area of the city (Tsukada *et al.* 2000). High infection rates of 'city foxes' increase the probability of transmission to pet dogs and cats (via rodents in parks and recreational areas). Specific studies were performed in Europe, in Stuttgart, Germany (mean prevalence 17%) (Romig *et al.* 1999), Zurich, Switzerland (prevalence ranged from 44% in urban foxes to 67% in foxes from the outskirt) (Hofer *et al.* 2000) and Geneva, Switzerland (mean prevalence 40%) (Romig *et al.* report of the Echinorisk programme to the European Commission; and Fisher, personal communication). The data show that *E. multilocularis* infection does exist in foxes living in the public parks located in the centre of cities, but the prevalence is rather low (under 30%); it may reach up to 75% in the public or private parks of the suburban areas, on the city territory (Romig *et al.* 1999). The actual risk for urban populations is still unknown. It is, however, clear that permanent presence of *E. multilocularis* eggs in urban environments and especially in recreational areas where children may play, could lead to a major change in the epidemiology of the disease. Complementary studies are currently performed in big cities of various countries and in smaller cities of the endemic areas in Germany, Switzerland, Austria, Czech Republic and France.

Socio-economic factors, deforestation, overgrazing and emergence of AE cases

Various economic and political reasons have led to deforestation in PR China. Field and Geographic Information System-aided studies have revealed a significant relationship between occurrence of high densities of rodents, increase in the surface of shrub and scrub-lands after deforestation and high prevalence of AE in humans in central China (Gansu, Ningxia) (addressed in detail by Giraudoux *et al.* in this supplement). The extremely high number of cases in these areas could have been directly related to a specific environment at a given period of time. Disappearance of the main source of contamination (dogs) and either reforestation or conversion of shrub and scrub-lands to ploughed lands could as well lead to an interruption of the parasite cycle and transmission to humans. Follow-up of this quasi-experimental situation should give interesting insights into the complex landscape/animal hosts/humans interplay which underlies AE epidemiology in humans.

A preliminary exploratory analysis of risk factors for AE transmission in Qinghai–Tibetan plateau of China has suggested that partial fencing around the settlements in winter pastures might promote AE prevalence rate in Tibetan herdsmen villages. A significant correlation was recently found between the surface of fenced areas and the prevalence of AE in 11 villages of Shiqu County, Ganzi Tibetan autonomous prefecture, Sichuan province, PR China (Wang *et al.* 2003). The underlying reason may lie in the overgrazing, an assumed cause of a population outbreak of small mammals in Qinghai–Tibetan plateau, which was exacerbated by the reduction of common grassland due to partial fencing nearby the settlements. In Tibetan herdsmen communities, grassland is roughly split into summer and winter pastures. From October to the next early May, the herdsmen stay in winter settlements and the livestock grazes in winter pasture. From early or middle May to late September, the majority of livestock grazes in summer pasture. At the beginning of the 1980s, the tenure of winter grassland was distributed to group-based individuals (group tenure). The herdsmen collectively use the group tenure pasture and their houses are usually set up near each other for security and mutual aid. Within the group tenure pasture, fenced areas are owned exclusively by individuals. Overgrazing is considered to be a key factor of grassland degradation and an assumed reason of population outbreak of small mammals, especially *Ochotona* spp. (Hou, 2001). It is generally assumed that a higher ratio between the number of livestock and the area of grassland means higher grazing pressure. However, grazing behaviour, controlled by humans, should also be taken into account. Further researches should pay attention to this issue.

CONCLUSION

Several examples show how changes in economic status, regulations and policies may generate conditions that favour interactions between animal hosts and maintenance of the parasite cycle. Epidemiological studies on alveolar echinococcosis performed in the past 30 years have stressed the various links between apparently unrelated collective decisions which resulted in changes in landscape, thus in rodent densities, and the emergence of the disease. Deforestation in China, suppression of ploughed fields and hedges in mid-mountain areas in Europe are other examples. On the other hand, individual or community-related human behaviour may also strongly influence the occurrence of contacts with the infecting parasite eggs, through attitudes towards wild animals, in rural as well as urban areas, contacts with domestic animals, or food.

Alveolar echinococcosis in humans is the overall result of a complex network of interactions between genetic, biological, behavioural, sociological, economic and political factors; this indicates that a multidisciplinary approach is not only fruitful but quite necessary to elucidate the reasons of its occurrence in humans and to plan for prevention.

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USE OF DISABILITY ADJUSTED LIFE YEARS IN THE ESTIMATION OF THE DISEASE BURDEN OF ECHINOCOCCOSIS FOR A HIGH ENDEMIC REGION OF THE TIBETAN PLATEAU

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Abstract. Shiqu County, located on the Tibetan plateau of western China, has an extremely high prevalence of both human alveolar echinococcosis (AE), and cystic echinococcosis (CE). The short form 12 version 2 quality of life survey, which was used to evaluate the extent to which morbidity associated with echinococcosis should be accounted, verified that there was a significant reduction in the mean health scores in all categories for individuals diagnosed with abdominal echinococcosis compared with an age and sex cross-matched population. Results of a larger ultrasound survey, which screened 3135 subjects, demonstrated that the prevalence rates of AE and CE were both approximately 6% with a combined prevalence rate of 11.4%. Prevalence rates adjusted for the age and sex structure of Shiqu County were 4.6% for AE and 4.9% for CE with an estimated overall adjusted prevalence rate of 9.5%. The burden of disease associated with echinococcosis was calculated using disability adjusted life years (DALYs) based on these estimated prevalence rates. Monte-Carlo techniques were used to model the uncertainty in the prevalence estimates and the disability weights. Using these methods, we estimated that the total numbers of DALYs lost due echinococcosis was 50,933 (95% confidence interval [CI] = 41,995–61,026). The DALYs lost consisted of approximately 32,978 (95% CI = 25,019–42,422) due to AE and 17,955 (95% CI = 14,268–22,128) due to CE and suggests an average of approximately 0.81 DALY lost per person. This study has clearly shown that the impact of DALYs lost due to echinococcosis, in terms of medical treatment costs, lost income, and physical and social suffering, is likely to be substantial in this highly endemic region of China.

INTRODUCTION

Human cystic echinococcosis (CE) and alveolar echinococcosis (AE) are caused by the larval stage of the taeniid tapeworms *Echinococcus granulosus* and *E. multilocularis*, respectively, and are among the most deadly helminth diseases known to humans. Cystic echinococcosis produces space-occupying lesions, usually in the liver or lungs, whereas AE results in highly infiltrative lesions of the liver and may give rise to metastases.[1] Expenses and loss of health and vitality associated with *Echinococcus* infection can become a significant burden not only for the affected individual and his or her family, but also for the community as a whole. The Tibetan plateau region of western China has been found to have one of the highest prevalences of both human CE and AE in the world.[2]

Potential impact of the disease on afflicted individuals must be taken into consideration when constructing a disability adjusted life year (DALY) estimate. A health survey is a useful tool with which to evaluate the physical and mental health state of a person with, in this instance, echinococcosis compared with a control population. Two previous studies suggested that patients surgically treated for CE had a significant decrease in the quality of life.[3,4] Subjects presenting for treatment have also been reported as having a substantially higher rate of unemployment.[5] However, to evaluate the societal burden of disease it is important to understand the effect that CE and AE have on previously undiagnosed individuals. The short-form 12 (SF-12) version 2 health survey is a generic measure of general health and well-being that can be used to evaluate the extent to which morbidity, associated with echinococcosis, should be accounted.[6] Therefore, the quality of life of individuals who were found to be abdominal ultrasound positive for either AE or CE on a cross-sectional study of the population of Shiqu County (Sichuan Province, People's Republic of China) was compared with negative individuals using this instrument. It is essential to know such information about the morbidity effects of echinococcosis before the numbers of DALYs lost due to the disease can be estimated.

The DALYs were first constructed for the Global Burden of Disease Study, which was developed to attempt to quantify the worldwide burden of disease attributed to 107 causes by sex and age.[7,8] This technique considers the impact of both premature mortality and morbidity caused by a disease state and can then be used to evaluate the economic impact of the disease on the community as well as the potential cost-effectiveness of intervention strategies. Human echinococcosis was not evaluated in the Global Burden of Disease Study.[7,8] Therefore, DALYs have been constructed for both AE and CE and applied to a region of the Tibetan plateau (Shiqu County, Sichuan Province).

MATERIALS AND METHODS

The SF-12 version 2 health survey. The SF-12 version 2 health survey (QualityMetric, Inc., Lincoln, RI) was used in this study due to its brevity and ease of use. Eight domains, or scales, of health are assessed in the survey: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. These domains were chosen from among 40 recommended in the Medical Outcomes Study and are considered among the most frequently measured health concepts.[9] In addition, two component scores, the Physical Component Summary (PCS) and the Mental Component Summary (MCS) were evaluated. The translation of the American English version of the SF-12 version 2 into Tibetan was undertaken according to the International Quality of Life Assessment protocol, which involved forward and backward translation and testing on a small pilot study.[10] In addition, appropriate wording substitutions were made that embodied similar concepts and health requirement levels, but were more familiar to the survey subjects.[11] Scoring of the SF-12 version 2 health survey was undertaken in accordance with standard procedures.[6]

Subjects. From 2001 to 2003, 3,135 subjects were examined using abdominal ultrasound as part of an echinococcosis screening and epidemiologic survey for Shiqu County, which has an estimated population of 63,000.[12] Prevalence estimates and an age profile, of the screened population, were calculated from the results of the ultrasound survey. The age profile of the screened population was then compared with the most recent census of the population of Shiqu County and an adjusted number of cases, expected from the 3,135 subjects if they had the same age profile as the total population, was calculated.[13] The adjusted prevalence for echinococcosis was then determined accordingly. Consent was obtained from all participants and individuals shown to be echinococcosis positive, based on World Health Organization diagnostic criteria, were provided free of charge with albendazole tablets as well as informed of their surgical options.[14,15] Ethical approval for all work carried out in China was obtained from the Medical Sciences Expert Consultant Committee, Sichuan Provincial Health Bureau, Sichuan Province (People's Republic of China). During April 2003, the Tibetan version of the SF-12 version 2 health survey was administered to ultrasound survey participants with the assistance of local government and health officials. Since up to 75% of inhabitants of the Tibetan plateau are illiterate, the Tibetan questionnaire was administered orally to those partaking in the survey. There were 39 individuals, identified as being echinococcosis positive via abdominal ultrasound, who consented to participate in the study. A cross-matched population (n = 39) based on age and sex, drawn from those testing ultrasound negative, was then administered the survey and the results compared with those of the ultrasound-positive subjects. Results from the Tibetan plateau echinococcosis survey were also evaluated against the standardized 1998 United States norm.[6] All comparisons were made using a Student's *t*-test.

Construction of DALYs. The use of DALYs is an attempt to quantify the burden of a disease, in this case echinococcosis, for Shiqu County (Sichuan Province, People's Republic of China). The basic formula for DALYs lost by an individual is as follows

$$-\left[\frac{DCe^{-\beta a}}{(\beta + r)^2}\left[e^{-(\beta+r)(L)}\,(1 + (\beta + r)(L + a)) - (1 + (\beta + r)a)\right]\right]$$

where, r is a discount rate, β is an age-weighting parameter, C is an age-weighting correction constant, D is a disability weight, a is the age of the individual at diagnosis, and L is the time lost to disability or premature mortality.[7] Parameter values used were $r = 3\%$, $\beta = 0.04$, and $C = 0.16243$.[7,8] Disability weights (D), derived for AE and CE, were based on values for liver cancer obtained from the original Global Burden of Disease Study as well as from the Dutch Disability Weight Group, which produced a set of disability weights for use in a western European context.[16] Liver cancer was chosen for this purpose since, like echinococcosis, it causes a space-occupying mass and often results in similar clinical symptoms (Table 1).[17–20]

Life expectancy was based on the Japanese estimated life span, which is one of the longest known, and was used to standardize DALYs lost in accordance with the Global Burden of Disease Study.[7] A life expectancy of 82.50 years was, therefore, chosen for females and 80.0 years was chosen for males. A model life-table, West Level 26, was used to estimate expected longevity for each age, with a Chinese life-table used for comparison.[7,21] The general DALY formula was used in the construction of DALYs specific for AE and CE. The DALYs were constructed on the premise of solely chemotherapeutic therapy because this is the most common treatment modality for the region and in nearly all cases the only treatment currently available.

Analysis. A DALY for AE was developed with disability outcomes divided into five components (cured, improved, stable, worse, or death) based on the health survey as well as findings from past studies in which albendazole was used as the sole treatment of human AE (Table 2).[22–26] To model uncertainty, Monte Carlo techniques were used using PopTools software (Commonwealth Scientific and Industrial Research Organization, Sydney, Australia). From published data (Table 2), the results of chemotherapeutic treatment of 103 AE patients were used to construct a multinomial distribution for the likely outcome of treatment. Of these 103 subjects, there was an approximate probability of 4% of cure resulting from calcification and regression of the lesions. Patients in this category were assigned a disability weight of 0.200 (Dutch weight for clinically disease free cancer) for five years. A probability of approximately 27% was given for having mild disease (improved) with disability weight 0.200 (Dutch weight for clinically disease free cancer), a probability of approximately 41% was given for having disease equated to a disability weight of 0.239 (stable) (the Global Burden of Disease weight for pre-terminal liver cancer), and a probability of approximately 22% was given for severe disease equating to a disability weight 0.809 (worse) (the Global Burden of Disease weight for terminal liver cancer). Patients assigned to these three disease states were provided with a disability weight until the end of their expected lifespan based on a trinomial distribution. In addition, approximately 6% of the

TABLE 1

Comparison of the presenting clinical signs of alveolar echinococcosis (AE) and cystic echinococcosis (CE) of the liver with hepatocellular carcinoma (HCC)

Presenting clinical signs	Jaundice	Hepatomegaly	Mass-related pain	Lung involvement	Asymptomatic*	Reference
HCC (n = 336)	42.6%	83.9%	56%	3.2%	2.1%	17
AE (n = 30)	43%	23%	20%	3%	7%	18
AE (n = 76)	25%	14%	25%	7%	14%	18
AE (n = 33)	21%	76%	60%	9%	–	19
CE (n = 59)	7%	5%	42%	9%	36%	20

* These cases were found incidentally in patients without clinical signs (diagnosed by chance at necropsy, laparotomy, or during ultrasound examination for other reasons such as pregnancy). Other categories were diagnosed clinically and confirmed radiologically.

TABLE 2
Outcomes due to treatment of alveolar echinococcosis with albendazole

Number in study	Cured	Improved	Stable	Worse	Death	Reference
5	0	1 (20%)	2 (40%)	1 (20%)	1 (20%)	22
11	2 (18%)	0	5 (46%)	3 (27%)	1 (9%)	23
35	2 (6%)	4 (11%)	25 (72%)	4 (11%)	0	24
37	0	11 (30%)	10 (27%)	12 (32%)	4 (11%)	25
15	1 (7%)	12 (80%)	0	2 (13%)	0	26

patients were assigned the outcome of eventual death, which equates to a disability weight of 0.809 for 10 years followed by death. Using these probabilities, subjects from a population of 103 were repeatedly and randomly assigned to these five groups with the above probabilities to model the uncertainty associated with the results from a sample size of 103. Thus for AE, the proportion a_{AE} assigned to the cure category varied as $a_{AE} \times 103 \sim$ multinomial (103, 0.04), the proportion b_{AE} with disability weight 0.200 varied as $b_{AE} \times 103 \sim$ multinomial (103, 0.27), the proportion c_{AE} with disability weight 0.239 varied as $c_{AE} \times 103 \sim$ multinomial (103, 0.41), the proportion d_{AE} with disability weight 0.809 varied as $d_{AE} \times 103 \sim$ multinomial (103, 0.22), and the proportion e_{AE} assigned death in 10 years varied as $e_{AE} \times 103 \sim$ multinomial (103, 0.06), where $a_{AE} + b_{AE} + c_{AE} + d_{AE} + e_{AE} \equiv 1$.

Disability weights for CE were assigned in a similar manner based on the results of albendazole treatment of 547 patients from past studies (Table 3).[22,24,27,28] There were no fatalities reported in these studies due, in part, to the absence of long-term follow-up. Therefore, an approximate 1% fatality rate was assigned to account for cases that will likely progress. Therefore, the proportion a_{CE} assigned to the cure category varied as $a_{CE} \times 547 \sim$ multinomial (547, 0.47), the proportion b_{CE} with disability weight 0.200 varied as $b_{CE} \times 547 \sim$ multinomial (547, 0.35), the proportion c_{CE} with disability weight 0.239 varied as $c_{CE} \times 547 \sim$ multinomial (547, 0.13), the proportion c_{CE} with disability weight 0.809 varied as $d_{CE} \times 547 \sim$ multinomial (547, 0.04), and the proportion d_{CE} assigned to death in 10 years varied as $e_{CE} \times 547 \sim$ multinomial (547, 0.01), where $a_{CE} + b_{CE} + c_{CE} + d_{CE} + e_{CE} \equiv 1$.

A uniform distribution was used to subtract between 0 and 5 years from the age of abdominal ultrasound diagnosis to model the age of onset of morbidity rather than the age of detection provided by the ultrasound diagnosis. The uncertainty of the point prevalence estimates was modeled using a binomial distribution. Thus, the prevalence rate P_{AE} in the general population for AE was modeled as $P_{AE} \times N_t \sim$ binomial (N_t, N_{AE}/N_t), where N_t is the sample size that undertook ultrasound examination and N_{AE} were the adjusted number positive for AE. The prevalence rate P_{ACE} of abdominal CE was modeled as $P_{ACE} \times N_t \sim$ binomial (N_t, N_{ACE}/N_t), where N_{ACE} is the adjusted number that were positive for CE on abdominal ultrasound. In both cases of AE and CE, Nt = 3,135 (see above).

In addition, past studies have indicated that only approximately 75% of CE cysts are located in the liver, with a substantial proportion of cases suffering from pulmonary echinococcosis, which cannot be diagnosed with ultrasound techniques.[29] Therefore, to account for pulmonary and other cases of non-diagnosed CE, the prevalence of CE for the improved/stable/worse category was modeled as: $P_{CE} = P_{CE} \times \Gamma$, where $\Gamma \sim$ uniform (1.17, 1.33).

A spreadsheet model incorporating the DALY formula was constructed in Excel® (Microsoft, Redmond, WA). Monte Carlo routines were implemented to re-sample across the distributions 10,000 times to account for variability in disability weight and prevalence estimates. Individuals diagnosed with both AE and CE were categorized as having AE for analysis purposes. Disability weight assignment was assumed to be age independent since there is no evidence to suggest disparity in clinical presentation dependent on age of onset. Since the prevalence of AE and CE vary at the township level, an average was taken for the entire county and the age and sex distribution of patients identified in this study was applied at the county level.

RESULTS

The 39 questionnaires for echinococcosis-positive participants were completed in their entirety except for one missing response for each of the following questions: 3a, 3b, 4a, 4b, 5, 6a, 6b, and 6c. There were no missing responses for the control group. Of the 39 positive individuals, 26 (67%) were female and 13 (33%) were male. Patient ages ranged from 8 to 80 years. Of the females, 60% were less than 41 years of age and 39% of males were less than 41 years of age. Patients with CE made up 51% of the echinococcosis-positive group and patients with AE made up the other 49%. If an individual did not answer a question, the domain the question contributed to was not included in analysis for that person. Based on comparison of mean scores for the Shiqu County control

TABLE 3
Outcomes due to treatment of cystic echinococcosis with albendazole

Number in study	Cured	Improved	Stable	Worse	Death	Reference
58	14 (24%)	29 (50%)	15 (26%)	0	0	22
253	72 (28%)	129 (51%)	46 (18%)	6 (3%)	0	24
59	50 (85%)	5 (8%)	1 (2%)	3 (5%)	0	27
118	97 (82%)	6 (5%)	0	15 (13%)	0	27
59	25 (42%)	25 (4%)	9 (16%)	0	0	28

group and the United States norms, it was decided that the echinococcosis-negative group from Shiqu County was a better indicator of the standard to which echinococcosis-positive patients in the area should be compared. The CE-positive individuals were compared with AE-positive individuals for all eight domains of health. No significant difference was found ($P > 0.05$) between the two groups for any of the domains tested and it was, therefore, decided to combine the CE-positive and AE-positive persons into a single echinococcosis-positive group for further analysis.

Individuals with a positive diagnosis of *E. multilocularis* or *E. granulosus* infection had a significantly lower mean score for all eight areas of health (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) and the two component scores (PCS and MCS) compared with the cross-matched population from the same region ($P < 0.05$) (Figure 1). Males and females from Shiqu County were compared with an analysis for sex bias. Scores in all areas were within one standard error for both the control group and the echinococcosis-positive group. When echinococcosis-negative males were compared with echinococcosis-positive males, the control group scored higher in all categories ($P < 0.05$) except social functioning. Echinococcosis-negative females scored significantly higher than echinococcosis-positive females in all

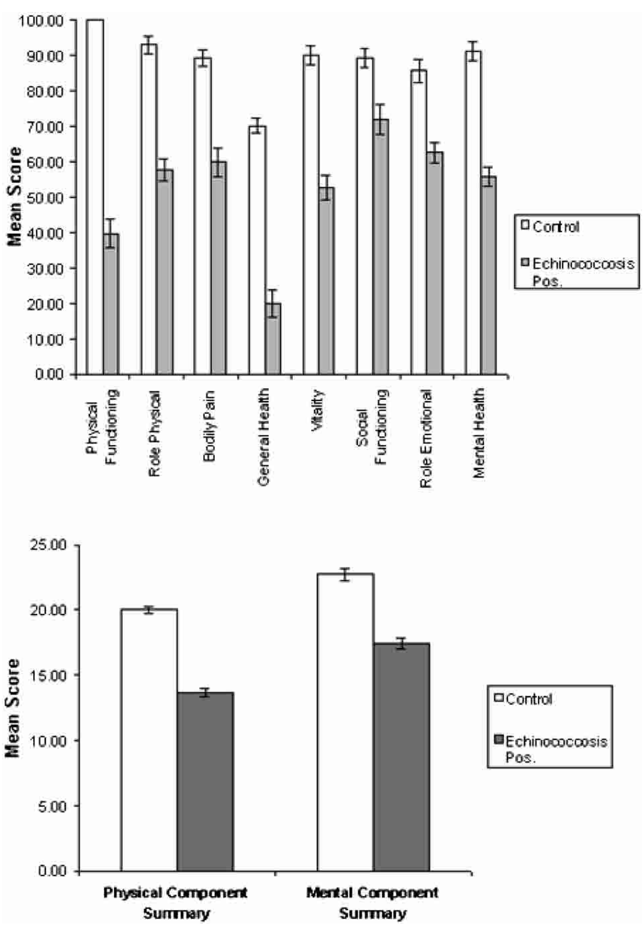


FIGURE 1. Mean Health Scores from the short form 12 version 2 health survey for echinococcosis-positive (Pos.) patients versus a control group from Shiqu County, Sichuan Province, People's Republic of China. Error bars show the standard error of the mean.

categories ($P < 0.05$). Individuals less than 41 years of age were compared with individuals greater than 40 years of age. When control groups and echinococcosis-positive groups were evaluated, it was shown that the older group, on average, scored the same or lower than the younger age group in all areas except for the vitality domain for the control group and the mental health domain for the echinococcosis-positive group. The only categories showing a significant difference, however, were bodily pain and role-emotional for the control group. Due to the findings of the SF-12 version 2 health survey, it was confirmed that human echinococcosis was associated with a decrease in the overall quality of life.

Of the 3,135 subjects examined with abdominal ultrasound, 178 cases were positive for CE (5.68%) and 180 cases (5.74%) were positive for AE (Figure 2). The distribution by age and sex of the screened population and total population is shown in Figure 3, with the total proportion of the screened population infected given in Figure 2. The estimated total adjusted prevalence was 4.6% for AE and 4.9% for CE, with an overall adjusted prevalence rate of 9.5%. Using the estimated adjusted variation of prevalence with age in Shiqu County and the West Level 26 life table, we estimated an echinococcosis burden of disease estimate of 50,933 (95% confidence interval [CI] = 41,995–61,026) DALYs lost the region (Figure 4). Alveolar echinococcosis contributed 32,978 (95% CI = 25,019–42,422) DALYs and CE contributed 17,955 (95% CI = 14,268–22,128) DALYs to the total value. This represents a loss of approximately 0.81 DALY per resident of Shiqu County due to echinococcosis or approximately 0.085 per person per 1% prevalence. When the data were fit to a Chinese life-table with a life expectancy of 68.85 years for males and 72.99 years for females, the total estimated DALYs lost for Shiqu county was 49,601 (95% CI = 40,781–59,446) (Figure 4).

DISCUSSION

Since disability weights have never before been assigned to human *Echinococcus* infection, it was therefore necessary to apply weights using the resources available to this study. A health survey was decided upon as one of the most attainable ways of showing a decrease in overall health of individuals with echinococcosis compared with the population norm. The SF-36 health survey has been used to indicate differences in health status between echinococcosis-positive individuals compared with a local cross-matched population.[3,4] In Jordan, individuals treated for CE scored significantly lower in the role physical and bodily pain categories, which was used as a justification for including morbidity costs in an economic model for the same region.[3] A similar study conducted in Wales showed a reduction in quality of life of individuals treated surgically for CE.[4] In contrast to the Shiqu County study, the Jordanian and Welsh participants had been treated for and were aware of their condition and its potential outcome. The physical impact of abdominal surgery may also have contributed to these patients' overall change in quality of life.[30] In contrast, the Shiqu County study allows for a pre-treatment evaluation of the association of morbidity with the condition itself. The SF-12 version health survey results for this study confirm that morbidity associated with echinococcosis needs to be considered, but do not prove that echi-

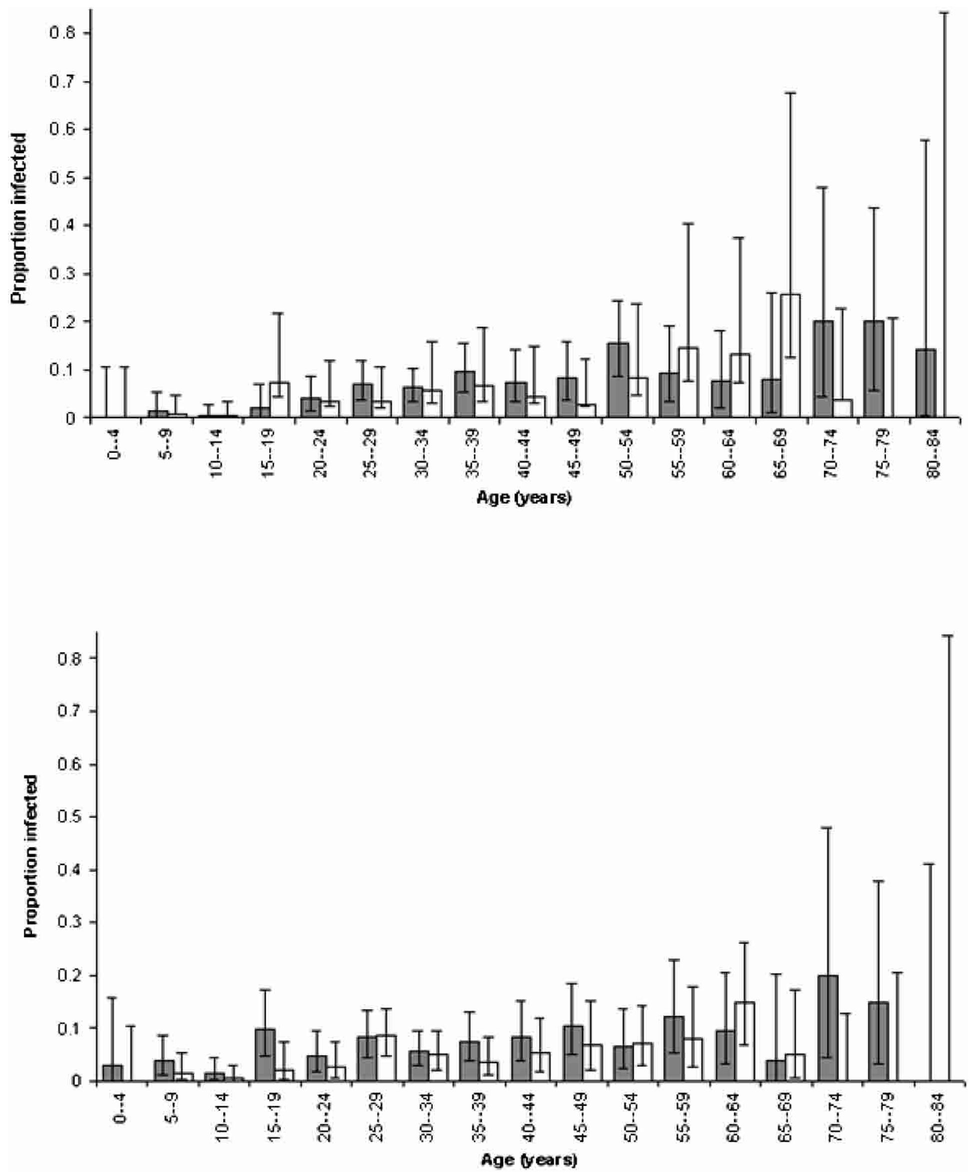
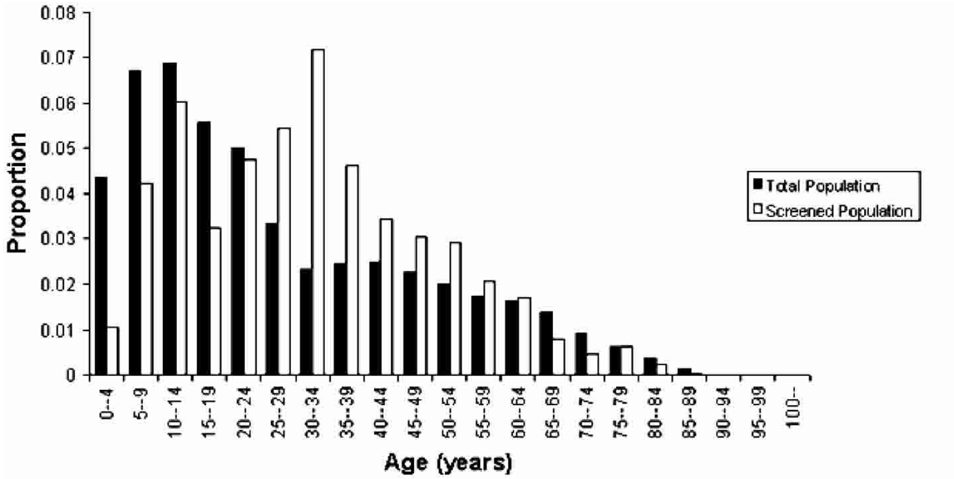


FIGURE 2. Proportion of the screened population infected by age and sex (Shiqu County, Sichuan Province, People's Republic of China). The upper graph represents cases of alveolar echinococcosis (with 95% exact binomial confidence limits) and the lower graph represents cases of cystic echinococcosis (with 95% exact binomial confidence limits). Females are represented in gray and males are represented in white.

nococcosis caused the decrease in the recorded quality of life. It is possible that subjects with a low quality of life are more susceptible to infection.

DALYs were decided upon as the most suitable measure of disease burden for this study, even though there has been controversy over the appropriateness of their use in the past.[31,32] One issue is the use of a single life table, based on the Japanese life span, being used over a vast range of populations where life expectancy may not be as high. In this study, using a Chinese life table resulted in a 2.6% decrease in the total number of DALYs lost due to echinococcosis. Another criticism directed at the DALY is that it assigns global disability rates without allowing for cultural or socioeconomic differentiation between tested populations.[33] The DALY, therefore, most likely undervalues the true disability caused by diseases and disabilities in developing countries. Others have argued that the DALY devalues the life of a disabled person and that age-weighting also devalues the lives of individuals on an un-grounded basis.[31,34] Even with these acknowledged obstacles, the DALY is still widely used and is generally acknowledged as one of the best ways in which to quantify an estimated measurement of morbidity and mortality from a given disease for a given population.

Deciding whether to incorporate mortality and cure into the DALY was another complexity, seeing that length of illness associated with AE and CE is extremely variable depending on location of the lesion or lesions as well as the rate at which the cyst grows or metastasizes. Without the benefit of surgical or chemotherapeutic treatment, the maximum life expectancy, after the time of diagnosis, for an AE patient is approximately 15 years.[35,36] In contrast, CE patients have the potential to live an extended period of time, with one case study reporting a patient who lived with latent CE for 53 years.[37] The mortality rate for untreated CE, however, is not



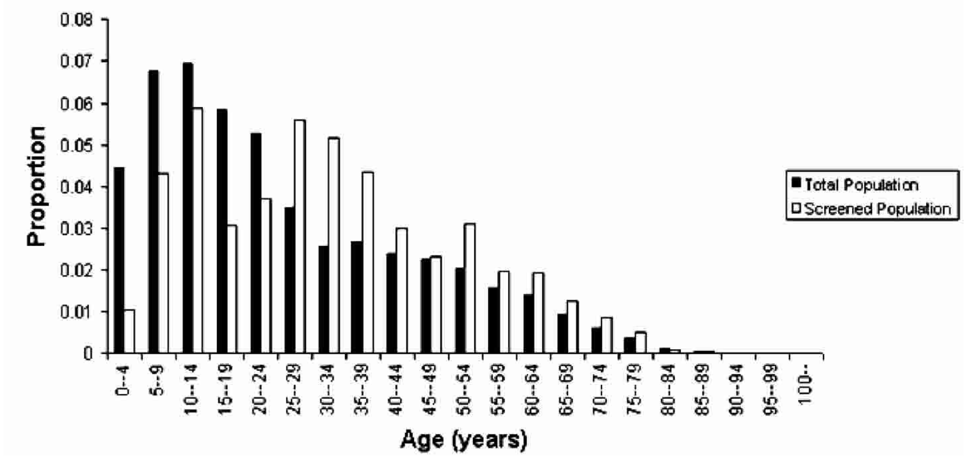


FIGURE 3. Distribution by age and sex of the screened population of Shiqu County, Sichuan Province, People's Republic of China versus the total population. The upper graph represents females and the bottom graph represents males.

known although operative fatality is estimated at approximately 2% or less.[1] Long-term fatality rates associated with CE and AE treated solely with albendazole also remain unknown since chemotherapy with benzimidazoles is still a relatively recent development. In addition, spontaneous calcification of lesions and cure as well as albendazole associated calcification and cure of both CE and AE have been reported and, therefore, included in the DALY estimation.[14,38,39]

Distribution of disability weights, consequently, proved to be challenging due to the varying clinical outcomes of the diseases, as well as the fact that methods used for assigning these weights in the past remain quite vague.[8] Disability weights for AE and CE were, therefore, assigned based on preceding articles reporting success and failure of treatment exclusively with albendazole. These reports were used only as a guideline, however, since many patients in these studies were deemed unlikely surgical candidates. In addition, previously reported studies have only followed patients for a short period of time and true disease-related death rates for these patients are likely to be greatly underestimated. The closest disease state for which a DALY was constructed for the Global Burden of Disease Study was liver cancer. Values for various stages of liver cancer were taken from both the Global Burden Disease Study as well as from the Dutch Disability Weight Group and applied to AE and CE. Although echinococcosis is a more chronic disease, the similar clinical symptoms justifies using these weights. However, echinococcosis would have fewer DALYs lost if compared with a population with a similar incidence of liver cancer due to the longer life expectancy of individuals with echinococcosis.

Assigning disability weights for AE and CE was also complex due to the large number of possible outcomes both with and without treatment as well as a wide range of primary lesion sites for CE. Not all CE cases become symptomatic and spontaneous cure has been reported due to calcification of the cyst, rupture of the cyst into the bile duct or bronchial tree with subsequent expulsion of the cyst material, or via collapse and resolution of the cyst.[1] In addition, CE cases with pulmonary cysts, which cannot be diagnosed via ultrasound, need to be taken into account.[29,40] This is especially true for high altitude areas, such as the Tibetan plateau, where lung-associated disease could be more clinically severe. Therefore, even when taking into account pulmonary CE, the estimated DALYs lost remains a conservative estimate. Unlike most

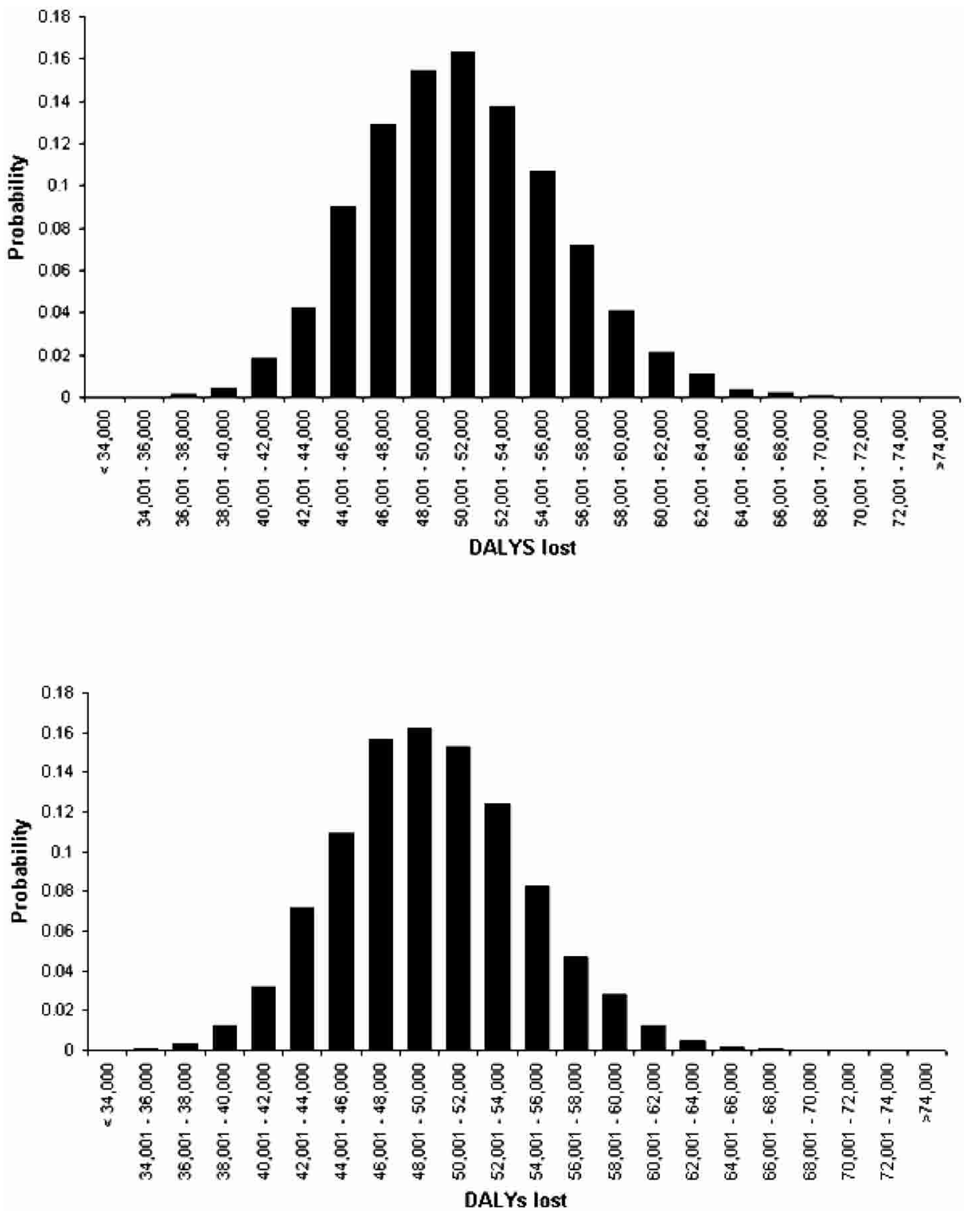


FIGURE 4. Frequency distribution of likely disability adjusted life years (DALYs) lost due to echinococcosis in Shiqu County, Sichuan Province, People's Republic of China using a Japanese life-table (**upper graph**) and a Chinese life-table (**lower graph**).

studies that have calculated the burden of other diseases, this report has attempted to take into account the uncertainty surrounding the data used to estimate disability weights and the prevalence rates of the diseases. By modeling this uncertainty using Monte-Carlo techniques, the construction of a probability density for the total number of DALYs lost has been achieved. Therefore, the assumptions described in this report are accounted for in the results given the uncertainty in the parameters. Such a stochastic approach is more useful than a deterministic approach calculating a single value for a point estimate because it gives an idea of the accuracy of the estimate of DALYs lost. The information obtained can then be used to assess the cost effectiveness of designing public health programs to control echinococcosis and to assess the risk of a poor return of DALYs saved for investment in such control programs.

The number of DALYs lost due to echinococcosis in this region is very high especially when acknowledging the potential undervaluation of DALYs in less developed parts of the world, such as the Tibetan plateau. The DALYs lost due to echinococcosis in Shiqu County is approximately 0.81 per person and compares unfavorably to the average DALY lost of 0.18 from the general Chinese population due to all disabilities evaluated combined, communicable and noncommunicable.[7] Findings for Shiqu County are, however, not typical for China. Shiqu County and its surrounding counties are especially prone to a high prevalence of echinococcosis due to the poor socioeconomic situation, local religious beliefs and customs, and the animal husbandry practices of the region.[2] Poor hygiene in addition to a close relationship with dogs, which have ready access to small mammals as well as offal from yaks, sheep, and goats helps contribute to the high prevalence of disease in humans. This study has clearly shown that the impact of DALYs lost due to echinococcosis, in terms of medical treatment costs, lost income, and physical and social suffering, is likely to be substantial. In addition, control options need to be considered to most efficiently decrease the incidence of AE and CE in the local population as well as decrease economic losses from *E. granulosus* infection in sheep, goats, and yaks. These issues will be addressed in a future publication.

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Titre de la thèse en Français

Aspects socio-économiques et éco-épidémiologiques de l'échinococcose alvéolaire dans les communautés pastorales tibétaines en république populaire de Chine.

Résumé de la thèse en Français

L'analyse multivariée des données chez 7138 sujets a montré que l'âge, dans tous les cas, prévenir le contact des mouches avec les aliments, chez les éleveurs, le nombre de chiens par famille, résider dans le Comté de Ganzi et posséder des peaux de renards, chez les agriculteurs, le sexe féminin, l'habitude de jouer avec les chiens et de boire de l'eau des ruisseaux, chez les urbains, étaient des facteurs de risque.

Par des questionnaires sur les pratiques d'élevage, des transects pour détecter les indices de présence de petits mammifères et mesurer les surfaces encloses, et la recherche du parasite dans les fèces des chiens, l'hypothèse de travail a été confirmée: le surpâturage des communaux était significativement associé à la surface des pâtures encloses ainsi qu'aux densités élevées de petits mammifères dans les communaux, elles-mêmes corrélées au niveau d'infection des chiens, susceptible d'expliquer les hautes prévalences de la maladie dans ces communautés pastorales Tibétaines.

Résumé de la thèse en Anglais

Multivariate analysis of data from 7,138 subjects revealed that increasing age, in all communities, “non-preventing flies from food” in herdsmen communities, “residence in Ganzi county”, “number of dogs kept” and “ownership of fox skin” in farmers’ communities, “female gender”, “drinking water from streams” and “playing with dogs” in urban communities were risk factors for Alveolar Echinococcosis in the respective populations.

Questionnaires on husbandry practices, transects to detect small mammal indices and measure the extent of fenced pastures, and assessment of dog infection confirmed our hypothesis that overgrazing in common pastures was significantly associated with the extent of fenced pastures in the winter settlements and appeared to increase the density of small mammals that may serve as reservoir for the parasite, which might in turn promote maintenance and transmission of *E. multilocularis,* through dog infection, in the Tibetan pastoralist communities of Sichuan, PR China.

Titre de la thèse en Anglais

Socio-economical and eco-epidemiological aspects of alveolar echinococcosis in Tibetan pastoralist communities in P.R.China

Mots-clefs Echinococcose alvéolaire; pratiques d'élevage; surpâturage; plateau tibétain; éco-épidémiologie; santé publique; analyses multivariées; *Ochotona curzoniae*